Agenda Item I(a)

California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

September 6, 2012

To: Enforcement Committee

Subject: Agenda Item I (a): Discussion Regarding the Process under Which the Board May Accept the Surrender of a License from a Licensee on Probation with the Board

FOR DISCUSSION AND POSSIBLE ACTION: The process under which the Board may accept the surrender of a license from a licensee on probation with the Board

Background

One of the standard terms and conditions of probation in the disciplinary guidelines allows for a licensee to request to surrender his or her license. Specifically:

> **License Surrender While on Probation/Suspension**
>
> Following the effective date of this decision, should respondent cease practice due to retirement or health, or be otherwise unable to satisfy the terms and conditions of probation, respondent may tender his or her license to the board for surrender. The board or its designee shall have the discretion whether to grant the request for surrender or take any other action it deems appropriate and reasonable. Upon formal acceptance of the surrender of the license, respondent will no longer be subject to the terms and conditions of probation. This surrender constitutes a record of discipline and shall become a part of the respondent's license history with the board.
>
> Upon acceptance of the surrender, respondent shall relinquish his or her pocket and wall license to the board within ten (10) days of notification by the board that the surrender is accepted. Respondent may not reapply for any license from the board for three (3) years from the effective date of the surrender. Respondent shall meet all requirements applicable to the license sought as of the date the application for that license is submitted to the board, including any outstanding costs.

Current Process

Currently, a licensee who wishes to surrender would send a letter to the board requesting to surrender his or her license pursuant to the license surrender term. The board, in turn, acknowledges the acceptance by way of letter. This current process does not allow the board to make the surrender a matter of public record for purposes of public disclosure.

As a result, when a probationer surrenders his or her license, the board has no formal document to reflect that the surrender has occurred.

Proposal

The attached Applications for Voluntary Surrender of a License (There are four of these, pharmacist/intern, pharmacy technician, designated representative, and premises) would provide the licensee with details related to the surrender. This document would become a public document that would be appended to the related Decision and Order on the board's Website.

Attachment I(a)

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APPLICATION FOR VOLUNTARY SURRENDER OF PHARMACIST / INTERN LICENSE

PLEASE PRINT IN BLACK OR BLUE INK OR TYPE YOUR RESPONSES

Name:	Case No.
Address of Record: _____ _____	

Pursuant to the terms and conditions of my probation with the California State Board of Pharmacy (Board) in Case No. _____, I hereby request to surrender my license, License No. _____. The Board or its designee shall have the discretion whether to grant the request for surrender or take any other action it deems appropriate and reasonable. Upon formal acceptance of the surrender of the license, I will no longer be subject to the terms and conditions of probation. I understand that this surrender constitutes a record of discipline and shall become a part of my license history with the Board.

Upon the acceptance of the surrender, I shall relinquish my pocket and wall license to the Board within ten (10) days of notification by the Board that the surrender is accepted. I understand that I may not reapply for any license from the board for three (3) years from the effective date of the surrender. I further understand that I shall meet all requirements applicable to the license sought as of the date the application for that license is submitted to the Board, including any outstanding costs.

PLEASE BE ADVISED THAT YOU ARE NOT RELIEVED OF THE REQUIREMENTS OF YOUR PROBATION UNLESS THE BOARD NOTIFIES YOU THAT YOUR REQUEST TO SURRENDER YOUR LICENSE HAS BEEN ACCEPTED.

_____ _____
Applicant's Signature Date

_____ _____
Executive Officer's Approval Date

All items on this application are mandatory in accordance with your probationary order and the Board's Disciplinary Guidelines as authorized by Title 16, California Code of Regulations section 1760. Failure to provide any of the requested information or providing unreadable information will result in the application being rejected as incomplete. The information provided on this form will be used to determine eligibility for surrender. The official responsible for information maintenance is the Executive Officer, telephone (916) 574-7900, 1625 N. Market Blvd., Suite N-219, Sacramento, CA 95834. The information you provide may also be disclosed in the following circumstances: (1) in response to a Public Records Act request; (2) to another government agency as required by state or federal law; or, (3) in response to a court or administrative order, a subpoena, or a search warrant. Each individual has the right to review the files or records maintained on them by our agency, unless the records are identified as confidential information and exempted by Section 1798.40 of the Civil Code.

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STATE AND CONSUMER SERVICES AGENCY
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APPLICATION FOR VOLUNTARY SURRENDER OF PHARMACY TECHNICIAN LICENSE

PLEASE PRINT IN BLACK OR BLUE INK OR TYPE YOUR RESPONSES

Name:	Case No.
Address of Record: _____ _____	

Pursuant to the terms and conditions of my probation with the California State Board of Pharmacy (Board) in Case No. _____, I hereby request to surrender my pharmacy technician license, License No. _____. The Board or its designee shall have the discretion whether to grant the request for surrender or take any other action it deems appropriate and reasonable. Upon formal acceptance of the surrender of the license, I will no longer be subject to the terms and conditions of probation. I understand that this surrender constitutes a record of discipline and shall become a part of my license history with the Board.

Upon the acceptance of the surrender, I shall relinquish my pharmacy technician license to the Board within ten (10) days of notification by the Board that the surrender is accepted. I understand that I may not reapply for any license, permit, or registration from the board for three (3) years from the effective date of the surrender. I further understand that I shall meet all requirements applicable to the license sought as of the date the application for that license is submitted to the Board.

PLEASE BE ADVISED THAT YOU ARE NOT RELIEVED OF THE REQUIREMENTS OF YOUR PROBATION UNLESS THE BOARD NOTIFIES YOU THAT YOUR REQUEST TO SURRENDER YOUR LICENSE HAS BEEN ACCEPTED.

_____ _____
Applicant's Signature Date

_____ _____
Executive Officer's Approval Date

All items on this application are mandatory in accordance with your probationary order and the Board's Disciplinary Guidelines as authorized by Title 16, California Code of Regulations section 1760. Failure to provide any of the requested information or providing unreadable information will result in the application being rejected as incomplete. The information provided on this form will be used to determine eligibility for surrender. The official responsible for information maintenance is the Executive Officer, telephone (916) 574-7900, 1625 N. Market Blvd., Suite N-219, Sacramento, CA 95834. The information you provide may also be disclosed in the following circumstances: (1) in response to a Public Records Act request; (2) to another government agency as required by state or federal law; or, (3) in response to a court or administrative order, a subpoena, or a search warrant. Each individual has the right to review the files or records maintained on them by our agency, unless the records are identified as confidential information and exempted by Section 1798.40 of the Civil Code.

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STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
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APPLICATION FOR VOLUNTARY SURRENDER OF DESIGNATED REPRESENTATIVE LICENSE

PLEASE PRINT IN BLACK OR BLUE INK OR TYPE YOUR RESPONSES

Name:	Case No.
Address of Record: _____ _____	

Pursuant to the terms and conditions of my probation with the California State Board of Pharmacy (Board) in Case No. _____, I hereby request to surrender my designated representative license, License No. _____. The Board or its designee shall have the discretion whether to grant the request for surrender or take any other action it deems appropriate and reasonable. Upon formal acceptance of the surrender of the license, I will no longer be subject to the terms and conditions of probation. I understand that this surrender constitutes a record of discipline and shall become a part of my license history with the Board.

Upon the acceptance of the surrender, I shall relinquish my designated representative license to the Board within ten (10) days of notification by the Board that the surrender is accepted. I understand that I may not reapply for any license, permit, or registration from the board for three (3) years from the effective date of the surrender. I further understand that I shall meet all requirements applicable to the license sought as of the date the application for that license is submitted to the Board.

PLEASE BE ADVISED THAT YOU ARE NOT RELIEVED OF THE REQUIREMENTS OF YOUR PROBATION UNLESS THE BOARD NOTIFIES YOU THAT YOUR REQUEST TO SURRENDER YOUR LICENSE HAS BEEN ACCEPTED.

_____ _____
Applicant's Signature Date

_____ _____
Executive Officer's Approval Date

All items on this application are mandatory in accordance with your probationary order and the Board's Disciplinary Guidelines as authorized by Title 16, California Code of Regulations section 1760. Failure to provide any of the requested information or providing unreadable information will result in the application being rejected as incomplete. The information provided on this form will be used to determine eligibility for surrender. The official responsible for information maintenance is the Executive Officer, telephone (916) 574-7900, 1625 N. Market Blvd., Suite N-219, Sacramento, CA 95834. The information you provide may also be disclosed in the following circumstances: (1) in response to a Public Records Act request; (2) to another government agency as required by state or federal law; or, (3) in response to a court or administrative order, a subpoena, or a search warrant. Each individual has the right to review the files or records maintained on them by our agency, unless the records are identified as confidential information and exempted by Section 1798.40 of the Civil Code.

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STATE AND CONSUMER SERVICES AGENCY
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APPLICATION FOR VOLUNTARY SURRENDER OF PREMISES LICENSE

PLEASE PRINT IN BLACK OR BLUE INK OR TYPE YOUR RESPONSES

Name:	Case No.
Address of Record: _____ _____	

Pursuant to the terms and conditions of probation against my premises license with the California State Board of Pharmacy (Board) in Case No. _____, I hereby request to surrender my premises license, License No. _____. The Board or its designee shall have the discretion whether to grant the request for surrender or take any other action it deems appropriate and reasonable. Upon formal acceptance of the surrender of the license, the premises will no longer be subject to the terms and conditions of probation. I understand that this surrender constitutes a record of discipline and shall become a part of the premises license history with the Board.

Upon the acceptance of the surrender, I shall relinquish my premises license to the Board within ten (10) days of notification by the Board that the surrender is accepted. I understand that I shall, among other things, submit a completed Discontinuance of Business form according to board guidelines and shall notify the board of the records inventory transfer. I may not reapply for any new licensure from the board for three (3) years from the effective date of the surrender. I further understand that I shall meet all requirements applicable to the license sought as of the date the application for that license is submitted to the Board.

PLEASE BE ADVISED THAT YOU ARE NOT RELIEVED OF THE REQUIREMENTS OF YOUR PROBATION UNLESS THE BOARD NOTIFIES YOU THAT YOUR REQUEST TO SURRENDER YOUR LICENSE HAS BEEN ACCEPTED.

_____ _____
Applicant's Signature Date

_____ _____
Executive Officer's Approval Date

All items on this application are mandatory in accordance with your probationary order and the Board's Disciplinary Guidelines as authorized by Title 16, California Code of Regulations section 1760. Failure to provide any of the requested information or providing unreadable information will result in the application being rejected as incomplete. The information provided on this form will be used to determine eligibility for surrender. The official responsible for information maintenance is the Executive Officer, telephone (916) 574-7900, 1625 N. Market Blvd., Suite N-219, Sacramento, CA 95834. The information you provide may also be disclosed in the following circumstances: (1) in response to a Public Records Act request; (2) to another government agency as required by state or federal law; or, (3) in response to a court or administrative order, a subpoena, or a search warrant. Each individual has the right to review the files or records maintained on them by our agency, unless the records are identified as confidential information and exempted by Section 1798.40 of the Civil Code.

Agenda Item I(b)

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STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

September 4, 2012

To: Enforcement Committee

Subject: Agenda Item I (b): Discussion Involving E-Prescribing of Controlled Substances

1. FOR DISCUSSION: The DEA's Electronic Prescribing Requirements and Verification Approved E-Prescribing Systems

In June 2010, the DEA's Interim Final Rule for the electronic prescribing of controlled substances took effect. There has been no adoption of a final rule yet.

The requirements are detailed and place requirements on prescribers and dispensers (and technology application vendors) who use electronic prescribing for controlled substances. A detailed explanation of the requirements was developed by the Board of Pharmacy and the Medical Board of California and is available on our board's web site: http://www.pharmacy.ca.gov/publications/eprescribing.pdf.

Excerpts are provided below, and a chart is provided in **Attachment 1(b)**.

The law requires in part:

1. Audit and Selection of Software Application(s)
   Before being used to create, sign, transmit, or process controlled substance prescriptions, electronic prescribing applications or pharmacy applications (stand-alone or integrated Electronic Medical Record (EMR) types) must have a third-party audit of the application certifying that it meets the requirements of the DEA regulations.

   The application provider must secure an audit from (1) a person/entity qualified to conduct a SysTrust, WebTrust, or SAS 70 audit; (2) a Certified Information System Auditor that performs compliance audits; or (3) a certifying organization whose certification process has been approved by the DEA.

   The auditor issues a report and/or certification to the application provider. The application provider must keep that report and/or certification for two years, and make it available to any prescriber or pharmacy that uses the application or is considering using the application. May be on provider's website.

Prescribers and pharmacies must review audit/certification report prior to using application to confirm that it performs the appropriate functions successfully. A prescription created using an application that does not meet requirements is invalid.

2. Identity Proofing of Prescribers (Practitioners) Identity proofing is the process by which a prescriber is uniquely identified, so that only that prescriber has the access necessary to authorize and sign electronic prescriptions using a software application. Identity proofing of prescriber must be done by an approved credential service provider (CSP) or certification authority (CA) [for digital certificates].

   Prescribers and pharmacies must review audit/certification report prior to using application to confirm that it performs the appropriate functions successfully.

   A prescription created using an application that does not meet requirements is invalid.

   Furthermore, both prescribers and pharmacies have an **ongoing responsibility** to immediately cease using an application (and ensure that any designated agents also cease using the application) if:
   - any required function of the application is disabled or appears to be functioning improperly;
   - the application provider notifies them that a third-party audit or certification report indicates that the application no longer meets DEA requirements; or
   - the application provider reports that the application is non-compliant.

3. Receipt and Processing of Prescription(s) by Pharmacies
   The pharmacy application must be certified by the third-party auditor to, among other things:
   - import, store, and display the information required for prescriptions;
   - import, store, and display an indication of signing transmitted by the prescriber;
   - import, store, and display the number of refills; and
   - import, store, and verify the prescriber's digital signature, where applicable.

   The second and the fourth of these listed requirements are particularly important to a pharmacy's proper verification of transmitted prescriptions.

The board had hoped that with respect to certification and audit requirements, that the DEA would post approved providers on its website. The board recently learned that the DEA does not currently intend to do such posting. As such, it will be the prescribers and pharmacies themselves that must ensure when e-

prescribing prescriptions, the systems and processes comply with the DEA's requirements.

As such, the board may ask for proof of use of appropriately audited and certified software during inspections of pharmacies that e-prescribe.

2. California HealthCare Foundation's Request for Proposals for a Pilot of the Electronic Prescribing of Controlled Substances

For a number of years, the California HealthCare Foundation has been vigorously promoting the use of e-prescribing for all prescription drugs in California. Despite the efforts of this group and others, e-prescribing in California is at a very low adoption rate compared with e-prescribing in other states.

To aid in implementation of e-prescribing systems for controlled drugs, the California HealthCare Foundation recent announced a request for proposals to support up to three pilot implementations of electronic prescribing systems in ambulatory provider organizations.

This RFP follows this page as **Attachment 1 (b)**

Attachment I(b)

California State Board of Pharmacy and Medical Board of California

Transmission and Receipt of Electronic Controlled Substance Prescriptions

Pursuant to DEA Interim Final Rule (IFR): Electronic Prescriptions for Controlled Substances

21 CFR Parts 1300, 1304, 1306, and 1311 (Fed. Reg. 16236-16319 (March 31, 2010)) – **effective June 1, 2010**

Who is affected: Prescribers; pharmacies; application providers. To participate, each category must:

Prescribers
Select application and ensure it meets DEA requirements
Apply for identity proofing
Set access controls
Sign (and archive) prescriptions

Pharmacies
Select application and ensure it meets DEA requirements
Set access controls
Process prescriptions
Archive prescriptions

Application Providers
Evaluate application(s) and/or reprogram as necessary
Undergo third-party audit or certification of software
Make audit/certification report available to users/possible users

Request for Proposals:

Pilot of the Electronic Prescribing of Controlled Substances

Deadline: Friday, September 28, 2012

Summary: Up to $150,000 is available to support up to three pilot implementations of the electronic prescribing of controlled substances in ambulatory provider organizations.

I. About the California HealthCare Foundation

The California HealthCare Foundation (CHCF) works as a catalyst to fulfill the promise of better health care for all Californians. The foundation supports ideas and innovations that improve quality, increase efficiency, and lower the costs of care. See more information at www.chcf.org.

II. Background

Electronic prescribing (e-prescribing or eRx) is a key technology that can improve the quality and efficiency of health care delivery. Despite this potential, California is consistently near the bottom in Surescripts' annual SafeRx rankings, which measure states' adoption and use of e-prescribing. One of the barriers to widespread adoption of eRx has been the prohibition, until recently, of the electronic prescribing of controlled substances (EPCS), which account for about 11% of prescriptions written annually.

In June 2010, the US Drug Enforcement Administration (DEA) issued an Interim Final Rule permitting EPCS, subject to stringent security and audit requirements (see http://www.gpo.gov/fdsys/pkg/FR-2010-03-31/pdf/2010-6687.pdf). For example, physicians can use only DEA-certified e-prescribing or electronic health record (EHR) systems; must complete identity-proofing processes; and must implement two-factor authentication to generate the electronic prescription. Pharmacies, pharmacy communication networks (such as Surescripts), and health IT vendors must comply with these requirements.

Despite the federal regulations now permitting EPCS, prescriptions for controlled substances continue to be sent via paper and fax. This creates significant workflow challenges for physicians as they must maintain parallel processes – a paper one for controlled substances and an electronic one for non-controlled medications. These dual workflows also create patient safety issues. A 2010 study found 37 errors for every 100 handwritten prescriptions, compared to 7 errors for every 100 electronic prescriptions. While the majority of these errors are not serious, it is estimated that about 7% have potential to do harm.

Physician and pharmacy interest in EPCS is growing. But given the limited adoption, it is unclear what challenges they may face when implementing EPCS. Some are concerned that they may be replacing an imperfect paper-based process with a cumbersome and largely untested electronic one.

III. Project Description

Purpose and Goals

The purpose of this project is to pilot EPCS in up to three ambulatory provider organizations (medical groups, community clinics, etc.) to better understand the issues and challenges with implementing federal regulations that affect physicians, community pharmacies (independent and chain), and the health information networks that enable the communication of prescription-related information. The goals are to identify implementation challenges and share the lessons learned broadly in California and nationally to facilitate the widespread adoption of EPCS.

Use of Grant Funds

Grants under this RFP can be used for a variety of purposes associated with implementing EPCS. These purposes include but are not limited to:

- Purchase or upgrade of computer hardware or software
- Purchase and implementation of security hardware or software
- Implementation services (such as technical, project management, or training)
- Completion of DEA-mandated identity-proofing process for prescribers
- Support for participating community pharmacy partners (including 340b pharmacies); for example, offsetting eRx-related transaction fees, identity proofing, etc.

It is anticipated that grants will be $50,000. Actual amounts will depend on the size and scope of selected projects.

Duration

The project will run about 12 months and has two phases: a nine-month pilot implementation (October 2012 – June 2013) and a three-month evaluation (July – September 2013).

Evaluation

American Institutes for Research (AIR) will conduct an independent evaluation of the project to capture implementation challenges and lessons learned. As a condition of accepting project funding, grantee organizations must participate in the evaluation process described in Section IX.

IV. Timeline

The table below shows key project dates.

Activity	Date
RFP Released	Wednesday, August 29, 2012 www.chcf.org/epcs
Webinar: CHCF RFP for Electronic Prescribing of Controlled Substances (Webinar recording to be posted within two days at www.chcf.org/epcs)	Thursday, September 6, 2012 1:00 PM Pacific http://chcfevents.webex.com/chcfevents/onstage/g.php?t=a&d=669326096 Password: chcf Conference Call In: 1-877-668-4493 Access Code: 669 326 096
Questions Due	Wednesday, September 12, 2012 5:00 PM Pacific
Questions Answered Online	Monday, September 17, 2012
Proposals Due	Friday, September 28, 2012 5:00 PM Pacific Email to epcsproject@chcf.org
Awards Announced	Monday, October 15, 2012

Questions about this RFP can be directed to Ronald Wacker, EPCS project manager, at ronwacker@yahoo.com, with the subject line "Questions re: EPCS RFP." Questions received after the September 6 webinar will be answered and posted online, along with the complete RFP, at www.chcf.org/epcs.

V. Eligibility

To be eligible for a grant under this RFP, the applicant must:

- Be an ambulatory provider organization (medical group, community clinic, or similar care delivery organization) in California
- Have been using e-prescribing for non-controlled substances for at least six months and/or have satisfied Stage 1 Meaningful Use requirements for e-prescribing measures
- Be using eRx/EHR software that is certified for EPCS or will be certified by the fourth quarter of 2012 per the requirements in §1311.300 of the federal regulations (see http://www.gpo.gov/fdsys/pkg/FR-2010-03-31/pdf/2010-6687.pdf)
- Be prepared to implement EPCS early in the fourth quarter of 2012

Organizations that participate in EPCS processes (such as eRx/EHR vendors or pharmacies) but are not eligible to receive funds directly are encouraged to work with eligible providers to apply.

VI. Proposals

Complete proposals should consist of:

1. Application cover sheet (available at http://www.chcf.org/grants/submitting-a-proposal).
2. Proposal Narrative: The narrative is limited to 12 pages with double-spaced lines in a 12-point font and one-inch margins.

   Note: The application cover sheet referenced above, all attachments, and the required budget form referenced below do not count toward the 12-page limit.

   The proposal narrative should include:

   a. Provider Organization Description: Including number of physicians, specialties, geographic locations in which services are provided, etc.

   b. Grantee Organization's Goals and Objectives: State the organization's purpose for the project and the specific goals and objectives it wishes to accomplish

   c. Health Information Technology (HIT) Experience: Describe the organization's experience with HIT including e-prescribing and EHRs, minimally including:

      i. The number/proportion of physicians that currently e-prescribe and the applicant's status on meeting Meaningful Use requirement for e-prescribing measures

      ii. How long physicians have been e-prescribing

      iii. The specific e-prescribing functionality/messaging types that have been implemented (initial prescriptions, renewal request responses, etc.)

iv. Other HIT that the organization has implemented (such as EHRs, practice management systems, HIE with third parties)

d. Implementation Plan: Describe the current status and plan for implementing EPCS, including:

i. The EHR/eRx software system that the organization has and that system's EPCS certification status

ii. If the organization is migrating to a new system or a new release of the existing system, identify the new EPCS-certified system

iii. Status of security-related efforts associated with EPCS including operationalization of two-factor authentication and identity proofing for prescribers, as well as procurement of security hardware/software (such as tokens)

iv. Any non-EPCS HIT software or functionality that the organization will be implementing during the grant period that may affect EPCS implementation

e. Pharmacy Trading Partners: Describe the following:

i. Pharmacies to which the organization will be transmitting prescriptions for controlled substances

ii. EPCS certification status of these pharmacies, if known

iii. Relative proportion of the organization's total prescriptions that are sent to these pharmacies

iv. Status of any discussions aimed at coordination and/or problem solving that the organization has had with these pharmacies regarding eRx generally and EPCS implementation specifically

f. High-Level Workplan: Outline a nine-month workplan for implementing EPCS, including but not limited to the number/proportion of physicians, by specialty and location.

g. Grantee Organization, Executive Leadership, Project Staff, Key Partners and Other Project Resources: Describe the qualifications of the organization to conduct the project, including identifying the executive leadership or sponsor for the project, the on-site project director, and any other key staff.

i. It is required that one individual be designated as the point of contact for CHCF staff, the EPCS project manager, and the evaluators

ii. Identify other key individuals representing partner organizations, including the eRx/EHR vendors and pharmacies

iii. Provide, as an attachment, a brief description or biography for each individual identified above, including his or her role at each organization

h. Budget Narrative: A description to accompany the Proposed Budget Form (see below) that should be consistent with item 2F, High-Level Workplan. Identify the financial and other resources that the organization and/or its partnering organizations plan to provide to the project.

3. Proposal Budget Form (available at http://www.chcf.org/grants/submitting-a-proposal).
   - Nonprofit organizations should use the "Line Item" Budget format
   - For-profit organizations should use the "Time and Materials" Budget format
4. Letters of Support: Formal letters of support for the application from partner organizations.

Applications must be submitted electronically to epcsproject@chcf.org by 5:00 PM Pacific on Friday, September 28, 2012. Receipt of proposals will be acknowledged by email.

VII. Selection Criteria

The following criteria will be used in the review process:

1. **Magnitude of local impact.** Priority will be given to applicants whose EPCS implementation will have a substantial impact in the local market such that local pharmacy readiness to participate is maximized (for example, the applicant's demonstrated influence in the community or its market share for outpatient prescribing).
2. **Robustness and feasibility of workplan**. Applicants should describe a robust and feasible plan for implementing EPCS during the nine months allowed.
3. **Leadership and resource commitment.** Applicants should demonstrate strong leadership commitment to implement EPCS through:
   a. Identification of key medical, administrative, and/or IT leadership for the project
   b. Dedication of necessary resources as demonstrated through a budget, including how grant funds will be used
4. **Readiness for EHR or eRx vendor to support EPCS.** Organizations should describe their EHR or eRx vendor's plans to support the specific regulatory requirements for EPCS within the project timeframe.
5. **Status of Discussions with Pharmacy Partners.** Applicants should identify the local partner pharmacies that are EPCS certified and indicate that discussions regarding coordinated implementation of EPCS have been conducted with these pharmacies.
6. **Experience with HIT, EHR, and eRx.** Applicants should demonstrate strong overall experience with HIT systems, in terms of both implementation and operation.

Additional criteria will include consideration of the extent to which applicants reflect diversity in terms of geography, type of provider organization, etc.

VIII. Expectations of Grantees

Grantees are expected to participate in key project activities, including but not limited to:

- Evaluation activities as described below
- Designation of an on-site project manager or coordinator as the key point of contact and an executive sponsor
- Kick-off meeting at CHCF's office in Oakland, California
- Monthly conference calls
- Submission of quarterly status reports
- Support for site visits by project staff
- Collaboration with other grantees, CHCF project staff, and other stakeholders on implementation issues such as sharing lessons learned

These expectations will be included in the grant agreement.

IX. Project Evaluation

American Institutes for Research (AIR) will manage a collaborative approach through which the following research questions are addressed:

- How were prescribing and pharmacy fulfillment workflows affected by the implementation of EPCS? What barriers and facilitators did each pilot site experience?
- Did participants perceive operational efficiencies and benefits that exceeded burden as a result of implementing EPCS? What data are available to support these perceptions?
- What lessons can other provider organizations and pharmacies considering EPCS learn from the pilots' experiences?
- What are the implications of your implementation pilot for policymakers and regulators, such as the DEA and the California Board of Pharmacy? Can opportunities be identified to streamline requirements for EPCS while maintaining adequate security protections?

To the extent feasible, AIR will incorporate into its report the results of several measures of EPCS adoption that are collected across the pilots; the measures under consideration are below.

Potential Evaluation Measure	Data Source
Total EPCS prescriptions (over time, by prescriber, specialty, etc.)	Point-of-care vendor and/or pharmacy
Total eRx prescriptions (over time, by prescriber, specialty, etc.)	Point-of-care vendor and/or pharmacy
EPCS transmission error rates, causes for errors, error notification time (schedule II vs. III-V)	Point-of-care vendor and/or pharmacy
EPCS vs. eRx "time to prescribe"	Provider organization
EPCS prescriptions as a % of total controlled substance prescriptions (pharmacy store/chain pharmacy-specific or individual prescribers, specialties, clinics)	Pharmacy; due to dependence on local pharmacy store collecting data, may be feasible only for limited time period
EPCS renewal requests vs. prescriber response (electronic renewal response or new EPCS)	Pharmacy and point-of-care vendor
EPCS vs. written controlled substance prescriptions; % involving call backs to prescribers for script clarification	Local pharmacy store

CHCF will publish results of the evaluation as part of its commitment to learning and transparency. Grantee organization will have the opportunity to review the results to ensure that the content is accurate and does not include legally protected or sensitive information. However, to ensure the independence of the findings, the evaluator will make the final decision on how to respond to any comments. (For more information on the typical elements in a CHCF evaluation report, see *Guidelines for Evaluation Reports* at http://www.chcf.org/grants/grantee-resources.)

AIR's evaluation will also require that grantees:

- Facilitate on-site visits at the start and finish of the pilot for AIR to interview the pilot's executive sponsor, on-site project manager, and other key staff
- Participate in a one-hour phone interview (primarily involving the on-site project manager) midway through the project
- Facilitate interviews with pharmacy partner personnel
- In coordination with participating pharmacies and the EHR/eRx vendor, generate and provide EPCS usage data needed to compute the pilot results
- Provide schematics reflecting pre-implementation and final EPCS workflows

X. For More Information

Direct questions regarding this RFP to Ronald Wacker, EPCS project manager, at ronwacker@yahoo.com. (NOTE: Applications should be submitted to epcsproject@chcf.org.)

Agenda Item I(c)

California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

September 5, 2012

To: Enforcement Committee

Subject: Agenda Item I (c): Nuclear Pharmacies and the Need for Interpreters

FOR DISCUSSION AND POSSIBLE ACTION: Request from a Nuclear Pharmacy for Clarification regarding 16 California Code of Regulations 1707.5(d) regarding Availability of Interpreters

Regulations adopted to implement California Business and Professions Code section 4076.5 regarding use of patient-centered labels for all prescription medication dispensed to patients in California, require the availability of interpreters. Specifically:

> (d) The pharmacy shall have policies and procedures in place to help patients with limited or no English proficiency understand the information on the label as specified in subdivision (a) in the patient's language. The pharmacy's policies and procedures shall be specified in writing and shall include, at minimum, the selected means to identify the patient's language and to provide interpretive services in the patient's language. If interpretive services in such language are available, during all hours that the pharmacy is open, either in person by pharmacy staff or by use of a third-party interpretive service available by telephone at or adjacent to the pharmacy counter.

The board was recently asked if this paragraph applies to nuclear pharmacies. A nuclear pharmacy will compound product that is patient-specific, but it does not dispense the drug to the patient. Instead the drug is provided to the practitioner who will administer the drug.

In such case, does a nuclear pharmacy need to comply -- and have available – interpreter services for patients they never see?

Agenda Item II

California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
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STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
EDMUND G. BROWN JR., GOVERNOR

Date: **September 6, 2012**

To: **Enforcement Committee**

Subject: **Agenda Item II - Discussion on the Implementation of California's Electronic Pedigree Requirements for Prescription Medication**

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a. Presentations and Questions from the Pharmaceutical Supply Chain on Their Readiness to Meet California's Staggered E-Pedigree Implementation Schedule

Attachment II a

Up until late 2008 when California's e-pedigree requirements were amended to delay implementation until at least 2015, the Enforcement Committee held public discussions with the supply chain to discuss readiness issues. The committee resumed these discussions in early 2012.

At this meeting, the committee seeks presentations from individuals, entities and associations on issues affecting implementation of e-pedigree requirements, readiness to meet the staggered implementation dates, and supply chain security issues.

The board will also soon establish a section of the board's website to contain items related to e-pedigree. One section will be a question and answer section. Questions submitted to the board will be answered in this area.

Attachment II a contains an article on Brazil's efforts in serializing and tracking pharmaceutical products.

b. Update on the Status of Proposed Regulations to Specify a Unique Identification Number for Prescription Medication, and "Grandfathering" Provisions for Non-Pedigreed Dangerous Drugs

Attachment II b

At the board meeting held July 17, 2012, the board directed that a rulemaking be initiated to add new Article 5.5 in Title 16 of the California Code of Regulations related to Electronic Pedigree Requirements, and propose the addition of Sections 1747 and 1747.1. The first step to do this is to initiate a 45 day public comment period on the proposed requirements.

Rulemaking documents have been filed with the Office of Administrative Law for publication in the near future. Staff anticipates the "Notice" will be published in the ***California Regulatory Notice Register*** on Friday, September 21. If published on September 21, the 45-day public comment period would conclude on November 5.

The board will issue a "Subscriber Alert" when the Notice is published, and also will make the rulemaking documents available on the board's website. The language approved for Notice by the board is provided in **Attachment II b**, along with a copy of the FDA's guidance document for serialized numeric identifiers.

c. Discussion Concerning Elements for Possible Regulation Requirements to Permit Inference as Provided by California Business and Professions Code Section 4163.3

Attachment II c

Inference would allow a read of a single serialized number on a case or pallet to link with every serialized package within the case or pallet, without having to separately read and confirm the presence of each individual container. Inference is required because the numeric identifier that is likely to be affixed to a container will be a 2-D matrix code, which requires a line of sight scan.

Inference is referenced in Business and Professions Code Section 4163.3:

> ***4163****.3. (a) It is the intent of the Legislature that participants in the distribution chain for dangerous drugs, including manufacturers, wholesalers, or pharmacies furnishing, administering, or dispensing dangerous drugs, distribute and receive electronic pedigrees, and verify and validate the delivery and receipt of dangerous drugs against those pedigrees at the unit level, in a manner that maintains the integrity of the pedigree system without an unacceptable increase in the risk of diversion or counterfeiting.*
>
> *(b) To meet this goal, and to facilitate efficiency and safety in the distribution chain, the board shall, by regulation, define the circumstances under which participants in the distribution chain may infer the contents of a case, pallet, or other aggregate of individual units, packages, or containers of dangerous drugs, from a unique identifier associated with the case, pallet, or other aggregate, without opening each case, pallet, or other aggregate or otherwise individually validating each unit.*
>
> *(c) Manufacturers, wholesalers, and pharmacies opting to employ the use of inference as authorized by the board to comply with the pedigree requirements shall document their processes and procedures in their standard operating procedures (SOPs) and shall make those SOPs available for board review.*
>
> *(d) SOPs regarding inference shall include a process for statistically sampling the accuracy of information sent with inbound product.*

(e) Liability associated with accuracy of product information and pedigree using inference shall be specified in the board's regulations.

Invitation for Comment on Inference and Certification of Individual Package Units

At the June 2012 Enforcement Committee meeting, interested parties were encouraged to provide information and or presentations to the committee members on implementation issues, and on July 23, 2012, the board issued a notice inviting interested parties to submit to the board information on inference and certification of individual package units, for consideration for a possible future rulemaking. The board requested that comments be submitted on or before September 1, so that comments could be reviewed and considered at this meeting.

Attachment II c contains background documents, the board's invitation for comment, and comments received from interested parties.

Manufacturers

AMGEN Inc.
Apotex Corporation
EMD Serono
Generic Pharmaceutical Association (GPhA)
Johnson & Johnson
MERCK & Co., Inc.
Pfizer Inc.
Pharmaceutical Research and Manufacturers of America (PhRMA)

Wholesalers

Cardinal Health
Healthcare Distribution Management Association (HDMA)
Health Industry Distributors Association (HIDA)
McKesson Corporation
Medline Industries, Inc.
Pharmaceutical Distribution Security Alliance (PDSA)

Pharmacies

California Society of Health-System Pharmacists (CSHP)
National Association of Chain Drug Stores (NACDS) / California Retailers Association (CRA) / California Pharmacists Association (CPhA)

Other

National Council for Prescription Drug Programs (NCPDP)

d. General Discussion

e. 2013 Future Meetings **Attachment II e**

f. Closing Comments

Attachment II(a)

Pharmaceutical products traceability system pilot project in Brazil

ABSTRACT

In order to break the vicious circle in the pharmaceutical market in which illegalities imply serious risks to public health, ETCO (Instituto Brasileiro de Ético Concorrencial, the Brazilian Institute of Ethical Competition) and the companies linked to the Pharmaceutical Chamber have entered in a partnership with the government. And, in a combined effort, we tested a simple and efficient mechanism, which can electronically track the course of any and every drug sold in Brazil. This article describes the new legislation establishing the obligation of such traceability system, and the lessons learned of the pilot organised by ETCO in collaboration with ANVISA (National Agency of Sanitary Surveillance).

By **André Franco Montoro Filho**, **Patrícia Blanco**, and **Luiz Emílio Ferreira**, ETCO

The pharmaceutical market in Brazil

A study of the pharmaceutical market in Brazil conducted in 2005 by the McKinsey consultancy office and the Pinheiro Neto law firm, by ETCO's request, showed that the high degree of the existing informality severely damages the industry and society as a whole.

The study conclusion was that informality must be fought with a set of specific actions, including the implementation of a traceability and authentication system, which aims at allowing a follow-up of each step of the pharmaceutical products, from the plant to the final consumer.

In accordance with information provided by IMS Health (December 2008), the Brazilian pharmaceutical market accounts for more than one billion units of Ethical products and 600 million OTC drugs. According to companies' estimates, 500 million drugs are directly sold to hospitals. The whole pharmaceutical chain comprises approximately 450 companies, over 2,000 wholesalers and a huge chain of 56,000 retail pharmacies and drugstores.

Fighting counterfeiting in Brazil: legislative developments

The risks to the Public Health and the losses resulting from drugs manufactured in non-compliance with the norms and procedures adopted present incalculable dimensions. Brazilian authorities and companies have been long seeking for mechanisms to restrain illegality.

In July 2nd, 1998, the National Congress qualified the counterfeiting of pharmaceutical products and raw materials as hideous crimes against public health, as defined in the Law no. 9,677/98. In this same year, the Secretary of Sanitary Surveillance of the Ministry of Health enacted the Administrative Rule no. 802/98, which instituted the Control and Inspection System for the whole chain of pharmaceutical products. The popular raspadinha (a scratch-off label with a reactive ink that helps in the verification of the authenticity of the drugs), the inviolability of the packages and the identification of the batch number in commercial transactions are some of the innovations established by that norm.

In 2002, the Administrative Act RDC no. 320 established that the wholesalers of pharmaceutical products should start to execute the commercial transactions and circulation operations with sale bills that presented, mandatorily, the product's batch number.

In spite of those measures, the level of informality in the Brazilian pharmaceutical industry is still alarming. Along the whole year of 2008, ANVISA seized approximately 45 tons of unregistered, smuggled and counterfeited products. According to ANVISA, in the first semester of 2009, 316 tons of fake medicines were seized. Another important issue is the cargoes thefts in the Brazilian cities and highways. In 2007, approximately 11,700 cargoes were stolen across the whole country, according to information provided by NTC & Logística (National Association of Cargo Transportation and Logistics). The estimated figure for 2008 is even higher: 12,400.

In March 4th, 2008, ANVISA published the Public Consultation no. 8. aiming at receiving reviews and suggestions associated to the minimum requirements for the definition of mechanisms to track the pharmaceutical products chain and to guarantee their authenticity. The purpose was to identify solutions that could allow the implementation of systems of drug tracking and authentication in the whole chain of pharmaceutical products.

In January 14, 2009, the Law no. 11,903 was issued, which created the National System of Drug Control. The Bill was initially submitted by the Congresswoman Vanessa Grazziotin and carried out in the House of Representatives during two years.

The Law establishes the tracking of all kinds of drugs existing in the country, from their manufacture to their sale to the final consumer. The control will be performed by means of technologies for electronic capture, storage and transmission of data. Each product will have to display an exclusive identification code.

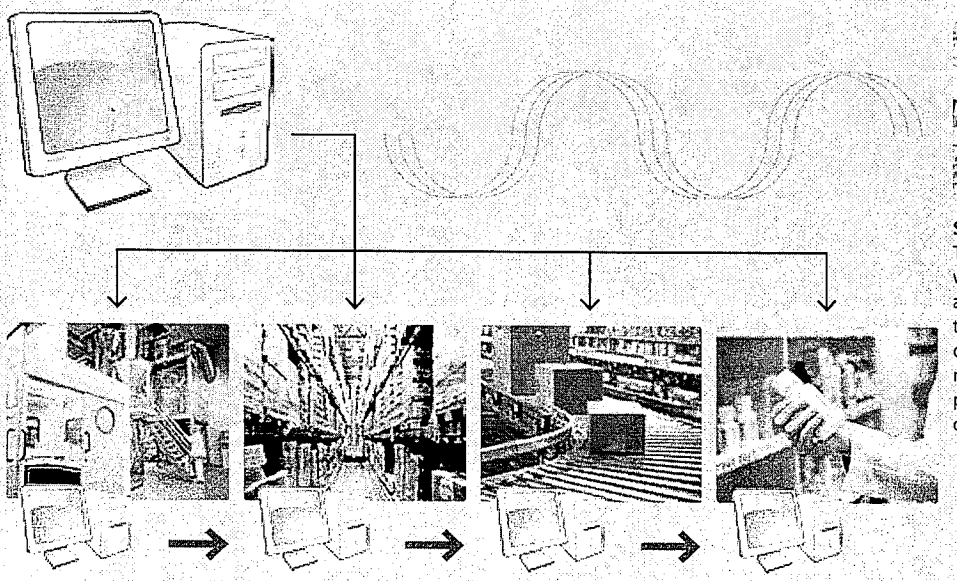
The law establishes that the system will have to be totally implemented within a period of three years. At the end of this period, the drug control in Brazil should reach levels of excellence, ensuring, in addition to the traceability, an effective monitoring about the drugs' use and prescription.

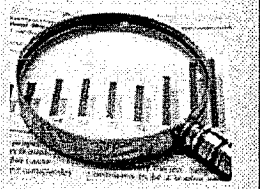
Enabling pharma traceability in Brazil: the pilot project

With the purpose of collaborating with ANVISA in the implementation of a tracking and authentication system, the ETCO's Pharmaceutical Chamber has submitted to the regulatory agency the proposition of developing a pilot project. The consolidation of efforts was discussed and the final agreement was signed in December 18, 2008.

From January to July 2009, ETCO conducted the pilot test of the Traceability System Pilot Project, supported by technicians from ANVISA. According to the Technical Cooperation Protocol, the Institute's work aimed at helping the regulating agency to define the best technological solution to effectively fight informality in the pharmaceutical industry.

System design





Surveillance
The Traceability System will ensure that inspection agents have access to traceability data for all drugs, from the point of manufacturing to the point of sales or point of dispense.

Industry
The manufacturer will be responsible for printing the Unique Drug Identifier (UDI) both on the secondary packages of its medicines and on logistic units (cases or pallets) – inference labels.[1] The code will contain the following information, initially sent to a private database and then to a central database:

- Product identification (GTIN);
- Batch number;

Warehouse
In case the manufacturer possesses its own warehouse, a product movement will occur previous to the billing, whose registration should be present in the database. A similar situation occurs when the company counts on an outsourced logistics operator. In this case, the following additional information should be sent to the central database:

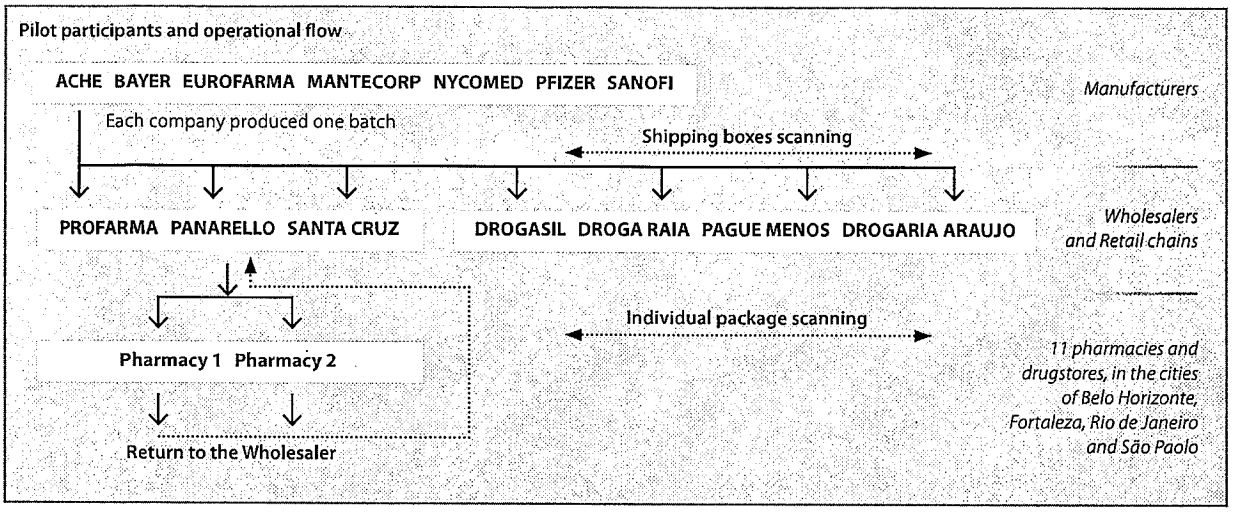
Wholesalers
As of receipt of the goods, the wholesaler will be accountable for transmitting other information, associated to the commercial transactions, to the central database:

- Date of the drugs arrival;
- Name of the retail pharmacy or drugstore.

Retail Pharmacy
The retailers will have to forward the following information to the central database:

- Data associated to the purchase of the goods;
- Data of sale to the final

[1] The working definition of "inference" as it applies here is that it refers to the ability to "infer", based on tracking and validation of a unique identifier attached to an aggregate package (e.g., pallet, case, tote) which has a hierarchicak relationship with unique



Pilot planning

The pilot test was established in different stages, in order to evaluate a significant representation of the industry's reality. In the first stage of the project ETCO´s group detected and mapped needs and expectations of its partners: companies, wholesalers and retailers. In the second stage, the practical section of the pilot test, which was put into operation in June 2nd, 2009, was executed. In the course of approximately 40 days, the processes of printing and scanning the identification codes on the secondary packages were assessed, and the collection and transmission of all information generated by the companies participating in the initiative was equally evaluated.

Pilot participants and operational flow

For the test an adequate volume of drugs was adopted (approximately 75 thousand) in order to support improvements and changes of route in the processes.

COMPANY	PRODUCT	AMOUNT
Aché (Biosintética)	BROMOPRIDE 1 mg/ml bottle w/ 120 ml	3,333
Bayer	ADALAT RETARD 10 mg w/ 30 tablets	29,800
Eurofarma	ASTRO 500 mg display w/ 60 tablets	1,650
Mantecorp	CELESTAMINE syrup 120 ml	9,600
Nycomed	RIOPAN suspension 240 ml	14,350
Pfizer	PONSTAN 500 mg w/ 24 tablets	14,000
Sanofi-Aventis	DORFLEX box w/ 30 tablets	3,000
	TOTAL	75,733

GS1 Brazil was responsible for the definition of international standards of coding, the entity acted as a certifier of the quality of the codes printed on the packages.

Open technological solutions of public domain were adopted to allow the required technical flexibility to meet the specificities of each company's processes.

- Adoption of several technologies for item marking: continuous ink-jet, laser and thermal ink-jet printers.
- Availability and flexibility so that the pharmaceutical chain's agents could select the equipment for the electronic capture of data (DataMatrix scanners) that was more compatible with their industrial and commercial processes.
- Equipment with low, medium and high speed and complexity, usually utilised by the whole pharmaceutical chain, was tested.
- Adaptation of the information technology systems of the pharmaceutical chain companies, so that the whole tracking process was put into operation in a validated form.

Adoption of an identification system, so that all essential information required for the tracking can be captured from each medicine package.

- The two-dimensional barcode, internationally accepted - GS1 DataMatrix (ECC 200), was adopted and printed on the secondary packages. The barcode included the following information about the product: GTIN, batch number, expiry date, and serial number.
- Usage of GS1-128 bar code with SSCC key on the logistic unit (case) to ensure the link with the content (secondary packs).

The data obtained during the test, from the manufacture to the point of purchase, were stored in a central database, allocated in a data center, in order to reflect what should occur in the real model. Every change of establishment was informed to the system in all of the tested stages: reception, incorporation to the inventory and sorting for the dispatch. The UDI lifecycle begins with the generation of a serial number and its storage in a database.

Lessons learned

- During the tests, no insoluble technical difficulty was detected in the implementation of the unitary coding technology in the manufacturers' packing lines.
- The choice of the adequate technology was based on the type of the manufactured products, the boxes' layout, the packing lines' speed, and the packing process, among other aspects.
- The available packing materials were used and some parameters of printing quality of the DataMatrix codes did not integrally comply with the GS1's recommendations. The tests showed, however, that occasional problems in the processes of code application and scanning are solvable.
- Regarding to the required equipment and software solutions, there are several companies in the market that can provide technologies complying with the specific demands of each link of the pharmaceutical chain.
- Investments on equipment, training courses and infrastructure should also be taken into consideration. Every professional directly involved in the production, storage and dispatching process should be trained in the traceability concept. They should understand that each box will be dealt with as a single package by the whole pharmaceutical chain.
- Important aspects were identified, which should be taken into consideration by the agents of the pharmaceutical chain and the regulatory authorities in order to ensure a greater efficiency in the implementation of the system.
- The mobilisation and gathering of forces of all of the key stakeholders, besides the support and availability for discussion from the federal government, are crucial for the definition of the best possible system, to be executed within the period established by law.
- The DataMatrix printing process was also tested in a logistics operator, where ink-jet printers and scanners were installed in a conveyor belt, out of the packing line, in which over 10 thousand boxes were printed and scanned. The test evidenced that, in a controlled environment, it is possible to obtain a printing level in the same standard found in the manufacturers' packing lines, taking into consideration the "Good Manufacturing Practices".

Conclusion

The purpose of ETCO's Pharmaceutical Chamber was to test a traceability system as close as possible to the reality of the pharmaceutical chain and to demonstrate its feasibility. The pilot project totally fulfilled its purpose of providing guidelines to all agents in the pharmaceutical chain for the implementation of the National System of Drug Control. The system can be implemented with the adoption of open technological solutions, of public domain, with characteristics and flexibility to be used by the companies regardless of their size. The pilot test showed the advantages of the direct printing model with open technologies.

The major paradigm change is the introduction of the "unitary codification", which is crucial for the achievement of the required tracking level for compliance with the Law.

About ETCO

Created in 2003 as a public interest entity of the civil society, ETCO's basic mission is to foster an ethics-based competition, fighting the competition unbalances generated by counterfeiting, tax evasion, smuggling and other business conduct deviations. Such practices result in illicit advantages for the transgressors, harming the companies that comply with the laws. Thus, the ethical companies find themselves discouraged to invest, to innovate and to grow, opening more room for illegalities.

ABOUT THE AUTHORS

André Franco Montoro Filho is Chairman of the Brazilian Institute of Ethical Competition – ETCO, a non-profit organisation that congregates non-government and entrepreneurial that aims to establish ethical parameters for competition. Mr. Montoro is Ph.D. in Economics from Yale University (USA), is full professor of the Economics and Administration College of the University of São Paulo (Brazil). He was Secretary of Economy and Planning of the State of São Paulo and President of the Brazilian Economic and Social Development Bank (BNDES) from 1985 to 1988.

Patrícia Blanco was Executive Director of ETCO – Brazilian Institute of Ethical Competition. Patricia was responsible for the management of the ETCO's project pilot of the pharmaceutical products traceability system.

Luiz Emílio Ferreira is Coordinator of the Pharmaceutical Chamber of ETCO – Brazilian Institute of Ethical Competition, which has worked with associated companies on the traceability system. Prior to joining ETCO, Luiz Emílio worked for more than 16 years in GlaxoSmithkline.

Attachment II(b)

Title 16. Board of Pharmacy
Proposed Language

Proposal to Add a New Article 5.5 and Article Title, and Add Sections 1747 and 1747.1 and Section Titles to Article 5.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

Article 5.5. Pedigree Requirements.

1747. Unique Identification Number.

For the purposes of Section 4034 of the Business and Professions Code, the "unique identification number" that is to be established and applied to the smallest package or immediate container by the manufacturer or repackager shall conform to requirements for Standardized Numerical Identifiers (SNIs) set forth in a March 2010 publication by the U.S. Food and Drug Administration (FDA) titled "Guidance for Industry, Standards for Securing the Drug Supply Chain – Standardized Numerical Identification for Prescription Drug Packages," (FDA'S Guidance Document), hereby incorporated by reference. As stated therein, an SNI consists of a serialized National Drug Code (NDC) product identifier combined with a unique numeric or alphanumeric serial number of no more than twenty (20) digits or characters. For dangerous drugs for which no NDC product identifier is assigned or is in use, an equivalent serialized product identifier may be used in place of the NDC consistent with the FDA's Guidance Document. This number shall be combined with a unique numeric or alphanumeric serial number that is not more than 20 digits or characters in length to establish the unique identification number.

This regulation shall become operative on January 1, 2015.

Note: Authority cited: Sections 4005, 4034, and 4163.2, Business and Professions Code. Reference: Sections 4034, 4034.1, 4163, 4163.1, 4163.2, 4163.4, 4163.5, Business and Professions Code.

1747.1. Specification of Pedigreed Dangerous Drugs; Specification of Existing Stock

(a)(1) To comply with Business and Professions Code section 4163.5, each manufacturer of a dangerous drug distributed in California shall submit to the board, by December 1, 2014, but no later than December 31, 2014, a declaration signed under penalty of perjury by an owner, officer, or employee with authority to bind the manufacturer, containing the following:

(A) A list and quantity of dangerous drugs by name and product package (SKU) type representing at least fifty (50) percent of the manufacturer's total that are ready for initial implementation of the serialized electronic pedigree requirements as of January 1, 2015;

(B) A statement identifying which one of the following methods was used to measure the percentage of drugs ready to be serialized: (i) unit volume, (ii) product package (SKU) type, or (iii) drug product family;

(C) A statement describing the calculation(s) used to arrive at the percentage figure of dangerous drugs ready for serialized pedigree requirements;

(D) A list and quantity of dangerous drugs by name and product package (SKU) type that are in the remaining percentage not yet ready to be serialized or subject to pedigree requirements; and,

(E) a statement specifying the technology employed to meet the pedigree requirements, including but not limited to any platform(s), vendor(s), hardware, software, and communication technologies deployed.

(2) To comply with Business and Professions Code section 4163.5, each manufacturer of a dangerous drug distributed in California shall also submit to the board, by December 1, 2015, but no later than December 31, 2015, a declaration signed under penalty of perjury by an owner, officer, or employee with authority to bind the manufacturer, containing the following:

(A) A list and quantity of its remaining dangerous drugs by name and product package (SKU) type that are ready for implementation of serialized electronic pedigree requirements as of January 1, 2016.

(B) A statement identifying which one of the following methods was used to measure the final percentage of drugs to be serialized: (i) unit volume, (ii) product package (SKU) type, or (iii) drug product family;

(C) A statement describing the calculation(s) used to arrive at the final percentage figure; and,

(D) A statement specifying the technology employed to meet the pedigree requirements, including but not limited to any platform(s), vendor(s), hardware, software, and communication technologies deployed.

(3) Any failure to submit to the board a declaration compliant with subdivision (a)(1) by December 31, 2014, any failure to submit to the board a declaration compliant with subdivision (a)(2) by December 31, 2015, or any failure to re-submit either declaration to the board in fully compliant form within ten (10) days after notice of deficiency by the board, shall constitute a violation of the Pharmacy Law.

(b) For the purposes of Business and Professions Code sections 4163.2 and 4163.4, any manufacturer, wholesaler or repackager seeking to designate dangerous drugs it possesses, owns, or controls that are not subject to the serialized electronic pedigree requirements, shall submit to the Board, by no later than August 1, 2016, a declaration signed under penalty of perjury by an owner, officer, or employee with authority to bind the manufacturer, wholesaler or repackager, containing the following:

(1) a list and quantity of dangerous drugs by name, product package (SKU) type and National Drug Code (NDC) product identifier in the possession, ownership, or control of the manufacturer, wholesaler or repackager that were acquired prior to July 1, 2016;

(2) a statement that specifies the means and source of acquisition; and,

(3) a statement that specifies the anticipated means of any subsequent distribution or disposition.

(c) For the purposes of Business and Professions Code sections 4163.2 and 4163.4, any pharmacy or pharmacy warehouse seeking to designate dangerous drugs it possesses, owns, or controls that are not subject to the serialized electronic pedigree requirements, shall submit to the Board, by no later than August 1, 2017, a declaration signed under penalty of perjury by an owner, officer, or employee with authority to bind the pharmacy or pharmacy warehouse, containing the following:

(1) A list and quantity of dangerous drugs by name, product package (SKU) type and National Drug Code (NDC) product identifier in the possession, ownership, or control of the pharmacy or pharmacy warehouse that were acquired prior to July 1, 2017;

(2) A statement that specifies the means and source of acquisition; and,

(3) a statement that specifies the anticipated means of any subsequent distribution or disposition.

(d) The Board or its designee shall have sole discretion to determine whether any of the declarations submitted pursuant to this Section are compliant, and to reject and require re-submission of any non-compliant declaration(s) until determined to be fully compliant.

Note: Authority cited: Sections 4005, 4034, 4163, 4163.2 and 4163.5, Business and Professions Code. Reference: Sections 4034, 4034.1, 4163, 4163.1, 4163.2, 4163.4, 4163.5, Business and Professions Code.

Guidance for Industry

Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages

FINAL GUIDANCE

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner (OC)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Office of Regulatory Affairs (ORA)
March 2010

Guidance for Industry

Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages

Additional copies are available from:
Office of Training and Communications
Division of Drug Information, WO51, Room 2201
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: 301-796-3400; Fax: 301-847-8714
druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
and/or

Office of Communication, Outreach, and
Development, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448
(Tel) 800-835-4709 or 301-827-1800
ocod@fda.hhs.gov
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
and/or

Office of Policy
Office of the Commissioner
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993
Phone: 301-796-4830

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner (OC)
Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research
Office of Regulatory Affairs

March 2010

Contains Nonbinding Recommendations

TABLE OF CONTENTS

Contains Nonbinding Recommendations

Guidance for Industry[1]

Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance is intended to address provisions set forth in Section 505D of the Federal Food, Drug, and Cosmetic Act (the Act) regarding development of standardized numerical identifiers (SNIs) for prescription drug packages. In this guidance, FDA is identifying package-level SNIs, as an initial step in FDA's development and implementation of additional measures to secure the drug supply chain.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of the Commissioner (OC), the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Office of Regulatory Affairs (ORA) at the Food and Drug Administration.

II. BACKGROUND

A. Food and Drug Administration Amendments Act of 2007

On September 27, 2007, the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85) was signed into law. Section 913 of this legislation created section 505D of the Federal Food, Drug, and Cosmetic Act, which requires the Secretary of Health and Human Services (the Secretary) to develop standards and identify and validate effective technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs. Section 505D directs the Secretary to consult with specific entities to prioritize and develop standards for identification, validation, authentication, and tracking and tracing of prescription drugs. The statute also directs that, no later than 30 months after the date of enactment of FDAAA, the Secretary shall develop an SNI to be applied to a prescription drug at the point of manufacturing and repackaging at the package- or pallet-level, sufficient to facilitate the identification, validation, authentication, and tracking and tracing of the prescription drug. An SNI applied at the point of repackaging is to be linked to the SNI applied at the point of manufacturing and, to the extent practicable, the SNI should be harmonized with international consensus standards for such an identifier. (See Section 505D(b)(2)). The provisions in section 505D(b) of the act complement and build upon FDA's longstanding efforts to further secure the U.S. drug supply. This guidance finalizes the draft guidance of the same title dated January 16, 2009 (74 FR 3054).

B. Scope of this Guidance

This guidance is intended to be the first of several guidances and regulations that FDA may issue to implement section 505D of the Act, and its issuance is intended to assist with the development of standards and systems for identification, validation, authentication, and tracking and tracing of

prescription drugs.[2] This guidance defines SNI for package-level identification only. For the purpose of this guidance, FDA considers the prescription drug package to be the smallest unit placed into interstate commerce by the manufacturer or the repackager that is intended by that manufacturer or repackager, as applicable, for individual sale to the pharmacy or other dispenser of the drug product. Evidence that a unit is intended for individual sale, and thus constitutes a separate "package" for purposes of this guidance, would include the package being accompanied by labeling intended to be sufficient to permit its individual distribution. For example, if a manufacturer's smallest unit of sale package is a container holding six drug-filled syringes, a single SNI would be the package-level identifier for the container holding the six drug-filled syringes; there would be no SNIs for the individual syringes, not intended by the manufacturer for individual sale. If a repackager then breaks that container down and repackages each syringe for individual sale, then the repackager must ensure that appropriate labeling accompanies each individual syringe[3] and a new and unique SNI would be the package-level identifier for each new package (e.g., each individual drug-filled syringe). SNIs applied to each new package by the repackager are to be linked back to the manufacturer's SNI for the container of six drug-filled syringes (505D(b)(2)).

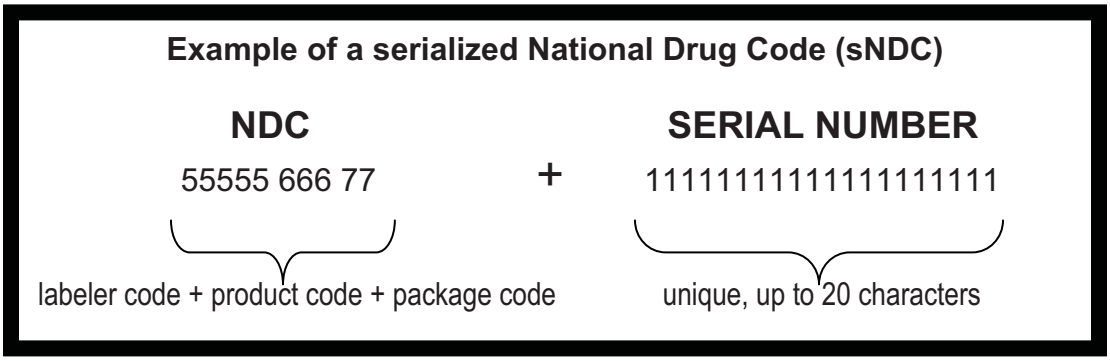
This guidance does not address how to link a repackager SNI to a manufacturer SNI, nor does it address standards for prescription drug SNI at levels other than the package-level including, for example, the case- and pallet-levels. Standards for track and trace, authentication, and validation are also not addressed in this guidance because this guidance only addresses the standardized numerical identifier itself and not implementation or application issues.

[2] Prescription drugs as defined in section 503(b)(1) of the act.
[3] See, e.g., Sections 502 (b) and (f).

III. STANDARDIZED NUMERICAL IDENTIFIERS

A. What should be a package-level SNI for most prescription drugs?

The SNI for most prescription drug packages should be a serialized National Drug Code (sNDC). The sNDC is composed of the National Drug Code (NDC) (as set forth in 21 CFR Part 207) that corresponds to the specific drug product (including the particular package configuration)[4] combined with a unique serial number, generated by the manufacturer or repackager for each individual package. Serial numbers should be numeric (numbers) or alphanumeric (include letters and/or numbers) and should have no more than 20 characters (letters and/or numbers). An example is shown below with a 10-character NDC.



B. What should be the package-level SNI for certain biological products that do not use NDC numbers?

Some prescription drugs approved under Section 351 of the Public Health Service Act, such as blood and blood components and certain minimally manipulated human cells, tissues, and cellular and tissue-based products (HCT/Ps), do not currently use NDC numbers. Examples of HCT/Ps that do not use NDC numbers include allogeneic placental/umbilical cord blood, peripheral blood progenitor cells, and donor lymphocytes for infusion. Instead, such products

[4]In the case of repackaged drugs, each package type should have an NDC that corresponds to the repacker or private label distributor for whom the drug is repacked and to the new package configuration.

currently use other recognized standards for identification and labeling, such as ISBT 128, which creates a unique identification number for each product package. See http://iccbba.org/about_gettoknowisbt128.html, "Guidance for Industry: Recognition and Use of a Standard for Uniform Blood and Blood Component Container Labels," (http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm073362.htm.) The SNI for these products should be the unique identification number created for each package under these other recognized standards, such as ISBT 128.[5]

C. Does the SNI include expiration date and/or lot or batch number?

Expiration date and/or lot or batch numbers are not part of the recommended SNI. Expiration date and/or lot or batch numbers are already accessible because FDA regulations require the inclusion of this information on the label of each drug product. (See 21 CFR §§ 201.17, 201.18, 211.130, 211.137, 610.60, and 610.61.) In addition, the SNI can be linked to databases containing this and other information. Addition of this information within the SNI will unnecessarily increase the length of, and introduce complexity into, the SNI. However, if a manufacturer or repackager chooses to include expiration date and/or lot or batch number with the SNI, it should ensure that the resulting number still permits users to distinguish and make use of the SNI. For example, expiration date and lot or batch number may be incorporated in accordance with the GS1 standards for use of Global Trade Item Numbers (GTIN)[6] (discussed below in Section F).

[5] FDA currently also recognizes Codabar as a standard for blood and blood component container labels. We note that ISBT 128 is becoming the more widely-used industry standard.

[6] See www.GS1.org -- Healthcare GTIN Allocation Rules (http://www.gs1.org/docs/gsmp/healthcare/GS1_Healthcare_GTIN_Allocation_Rules.pdf).

D. Why did FDA select the serialized NDC for package-level SNI for most prescription drugs?

FDA chose the sNDC as the package-level SNI for most prescription drugs because we believe that it serves the needs of the drug supply chain as a means of identifying individual prescription drug packages,[7] which in turn should facilitate authentication and tracking and tracing of those drugs. Most prescription drug product packages already have an NDC on them. By combining a serial number of up to 20 characters with the NDC, the sNDC should be sufficiently robust to support billions of units of marketed products without duplication of an SNI. This approach will allow manufacturers and repackagers to assign serial numbers to combine with the NDC for unique identification of individual product packages. The SNI can also be linked to databases containing such product attributes as lot or batch number, expiration date, distribution/transaction history information, and other identifiers related to a product. As already noted, defining the SNI is expected to be a first step to facilitate the development of other standards and systems for securing the drug supply chain. Many aspects of the implementation of package-level identification will take shape in the future, as the standards that make use of SNI are developed.

E. Should the SNI be in human- and machine-readable forms?

FDA believes that an SNI generally should be applied to each package in both human-readable and machine-readable forms. However, at this time, FDA is not specifying the means of incorporating the SNI onto the package. The SNIs described in this guidance are compatible with, and flexible for, encoding into a variety of machine-readable forms of data carriers, such as

[7] As described above, ISBT-128 and Codabar serve the same function for certain biologics that lack NDCs.

2-dimensional bar codes and radio-frequency identification (RFID),[8] leaving options open as technologies for securing the supply chain continue to be identified, and standards making use of SNI are developed. A redundant human-readable SNI on the package would provide the ability to identify the package when electronic means are unavailable (e.g., in the event of hardware/software failure). Due to the wide-variety of packaging required to accommodate different products and product integrity needs, FDA also is not specifying a location on the package where an SNI should be placed. If the NDC is already printed on the package in human-readable form, then the serial number could be printed in human-readable form in a non-contiguous manner elsewhere on the product package. Any SNI placed on the package must not obstruct FDA-required labeling information[9] and should be placed in a manner that allows it to be readily scanned/viewed without damaging the integrity of the packaging or product..

F. Is the SNI that FDA is recommending compatible with international standards?

In addition to facilitating other actions to secure the drug supply chain, adoption of the sNDC as the SNI for most prescription drugs, and of other recognized standards, such as ISBT 128, for certain biological products, satisfies the requirement in 505D(b)(2) that the SNI developed by FDA be harmonized, to the extent practicable, with internationally recognized standards for such an identifier. Specifically, use of an sNDC is compatible with, and may be presented within, a GTIN, which can be serialized using an Application Identifier (AI) (21) to create a serialized GTIN (sGTIN) for use with RFID or for certain barcodes.[10] GTIN is a global standard for item and object identification, established by GS1, a consensus-based, not-for-profit, international

[8] FDA's enforcement policy with respect to the application of current good manufacturing practices to RFID technology is provided in Compliance Policy Guide (CPG) Section 400.210. See http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074357.htm. This CPG would apply if an SNI were embedded into an RFID tag.

[9] See section 502(c) of the Act.

[10] See www.GS1.org -- Healthcare GTIN Allocation Rules (http://www.gs1.org/docs/gsmp/healthcare/GS1_Healthcare_GTIN_Allocation_Rules.pdf).

standards organization that works with manufacturers, distributors, retailers, and others in the drug supply chain. A GTIN may be used to uniquely identify items at the package level throughout the supply chain. FDA has been an active observer and participant in GS1 standards development related to healthcare and drug products. According to documentation from GS1, the GTIN is used worldwide by twenty-three industry sectors, including healthcare, and has been adopted by sixty-five countries to uniquely identify pharmaceutical products.

Attachment II(c)

California State Board of Pharmacy
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Phone (916) 574-7900
Fax (916) 574-8618
www.pharmacy.ca.gov

STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
EDMUND G. BROWN, JR., GOVERNOR

ISSUE DATE: July 23, 2012

Opportunity to Submit Information Necessary to Possible Board Rulemaking On Inference and Certification of Individual Package Units – Drug Pedigree Law

Pursuant to Business and Professions Code section 4163.3 (see below), the Board of Pharmacy is confirming its willingness to receive information by written submission regarding supply chain participants' ability to use or rely on inference(s) as to the contents of aggregate containers for purposes of certification of delivery or receipt of individual package units of dangerous drugs, as required by the California electronic pedigree law. (Bus. & Prof. Code, §§ 4034, 4163 et seq.)

To be considered for purposes of developing a possible future Board rulemaking on this subject, we request that all written submissions contain at minimum the information outlined below, and be received by mail or personal delivery at the Board offices by no later than September 1, 2012.

> **§ 4163.3. Legislative intent; maintaining integrity of pedigree system; use of inference**
>
> (a) It is the intent of the Legislature that participants in the distribution chain for dangerous drugs, including manufacturers, wholesalers, or pharmacies furnishing, administering, or dispensing dangerous drugs, distribute and receive electronic pedigrees, and verify and validate the delivery and receipt of dangerous drugs against those pedigrees at the unit level, in a manner that maintains the integrity of the pedigree system without an unacceptable increase in the risk of diversion or counterfeiting.
>
> (b) To meet this goal, and to facilitate efficiency and safety in the distribution chain, the board shall, by regulation, define the circumstances under which participants in the distribution chain may infer the contents of a case, pallet, or other aggregate of individual units, packages, or containers of dangerous drugs, from a unique identifier associated with the case, pallet, or other aggregate, without opening each case, pallet, or other aggregate or otherwise individually validating each unit.
>
> (c) Manufacturers, wholesalers, and pharmacies opting to employ the use of inference as authorized by the board to comply with the pedigree requirements shall document their processes and procedures in their standard operating procedures (SOPs) and shall make those SOPs available for board review.
>
> (d) SOPs regarding inference shall include a process for statistically sampling the accuracy of information sent with inbound product.
>
> (e) Liability associated with accuracy of product information and pedigree using inference shall be specified in the board's regulations.

Section 4163.3 affirms the base requirement of the California pedigree law that all participants in the dangerous drug supply chain will "verify and validate the delivery and receipt of dangerous drugs against [electronic] pedigrees at the unit level, in a manner that maintains the integrity of the pedigree system without an unacceptable increase in the risk of diversion or counterfeiting." Accordingly, the subsequent direction to the Board, to issue regulations defining circumstances under which it would be permissible to substitute an inference as to the contents of an aggregate container for verification and validation of that container's individual unit contents, is similarly limited. Any allowance for inference(s) cannot unacceptably increase supply chain risk(s).

To meet this standard, the Board must base any regulation permitting inference on supply chain information and data demonstrating that use or reliance on inference in specified settings and/or under particular transactional circumstances will not unacceptably increase supply chain risk(s).

At its public meetings, the Board has repeatedly stated its willingness to receive this information. This notification confirms that the Board will accept written submissions from interested parties, in support of or in opposition to permitting inference under specified circumstances, to develop the record necessary to any Board rulemaking on the subject of inference and/or certification.

Necessary Information in Submissions

Any submission by an interested party[1] should include at least the following:

1. Identifying and contact information for the submitting person or entity.

2. A description of the submitting party's interest in this subject, including the submitting party's role, if any, in the supply chain (e.g., manufacturer, repackager, distributor, or dispenser) or other basis for interest (e.g., vendor, consultant, standards body) and a brief description of the person, company, or other entity responsible for the submission.

3. If the submitting party is a supply chain participant, a detailed description of the means and methodology, including hardware and software specifications, processes, and data carrier(s), that the submitting party has deployed or intends to deploy to "verify and validate the delivery and receipt of dangerous drugs against [electronic] pedigrees at the unit level," including specification of the means and methodology for certification.

4. If the submitting party is seeking a regulatory allowance for inference, a specific request for same along with a detailed description of the particular circumstance(s) and/or those transaction(s) under which or pursuant to which there is a perceived need for inference. Define the requested inference(s) as specifically as possible, and where possible provide a limiting descriptor for such transaction(s) that could be used in regulatory language. In addition, provide as much data as possible regarding the factual circumstance(s) and/or transaction(s) in question, including the number and percentage of transaction(s) to which such an inference might apply, both with regard to the submitting party and in the supply chain as a whole, and any trading partners that will be involved in the inference(s).

5. If the submitting party is opposed to a regulatory allowance for inference, either generally or with regard to particular circumstances/transactions, a detailed description of same that as closely as possible meets the requirements of item 4., above.

6. The detailed reason(s) that such an inference is necessary and/or advantageous, and either decreases risk(s) of diversion or counterfeiting (or other risk(s) in the supply chain), holds risk(s) constant, or does not unacceptably increase such risk(s). Or the detailed reason(s) any inference(s) is/are unnecessary, disadvantageous, or unacceptably increase(s) risk(s).

[1] The Board expects that submissions will be made primarily by individual persons, companies, or other entities that are themselves involved in the supply chain and able to supply information and data specific to their own operations regarding the potential benefits and risks of inference(s). Although the Board also welcomes input from associations and other groups, it is most interested in the kind of detail that individual submissions can better provide. The Board is also interested in hearing from vendors, consultants, standards bodies, hardware and software providers, and other experts in the field, regarding their viewpoints on and experience(s) with the use of inference(s).

7. Proposed SOPs that incorporate and explain the use of the inference(s), and describe the proposed process for statistical sampling to ensure the accuracy of pedigree information.

8. A proposal for the allocation of any liability that may be incurred due to use of inference.

Where and When to Submit

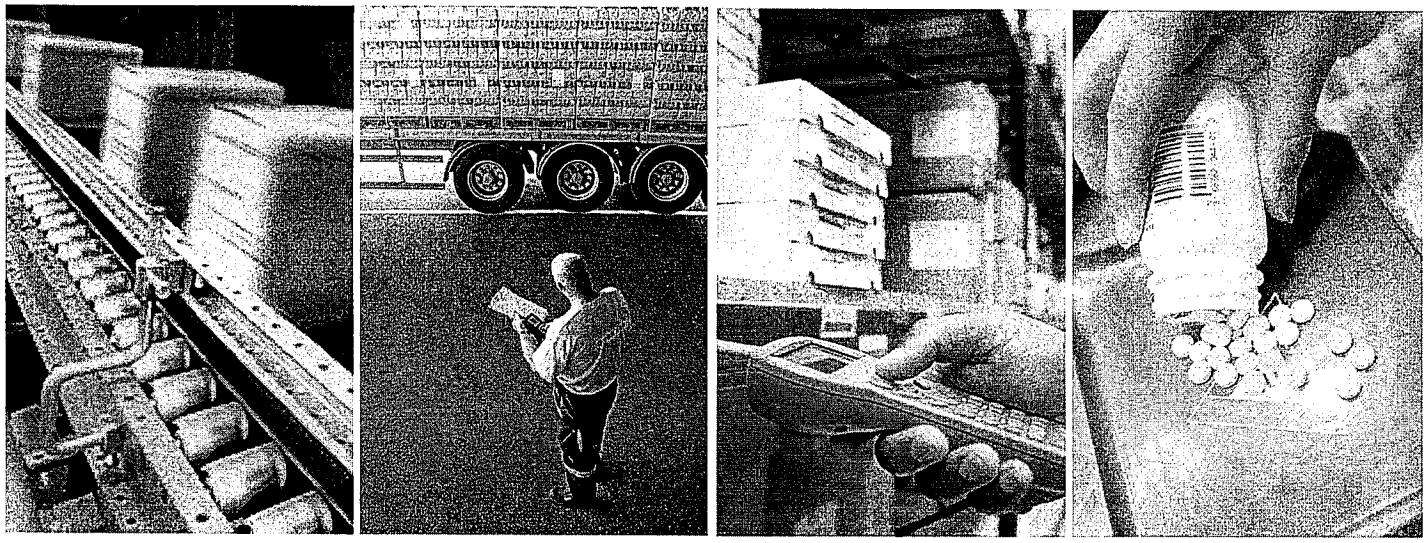
All written submissions should be mailed or delivered to Executive Officer Virginia Herold, Board of Pharmacy, 1625 N. Market Blvd., Suite N219, Sacramento, CA 95834. Materials received on or before September 1, 2012 will be considered by the Board in developing a possible rulemaking. These submissions will be considered at the Enforcement Committee meeting on September 11, 2012, and/or at the full Board meeting on October 25-26, 2012.

Inference and Certification of Individual Package Unit

Background Documents

GS1 Healthcare® US

Improving Patient Safety and Supply Chain Efficiency



The Practice of Inference

in the U.S. Pharmaceutical Supply Chain

RELEASE 1.0
May 2010

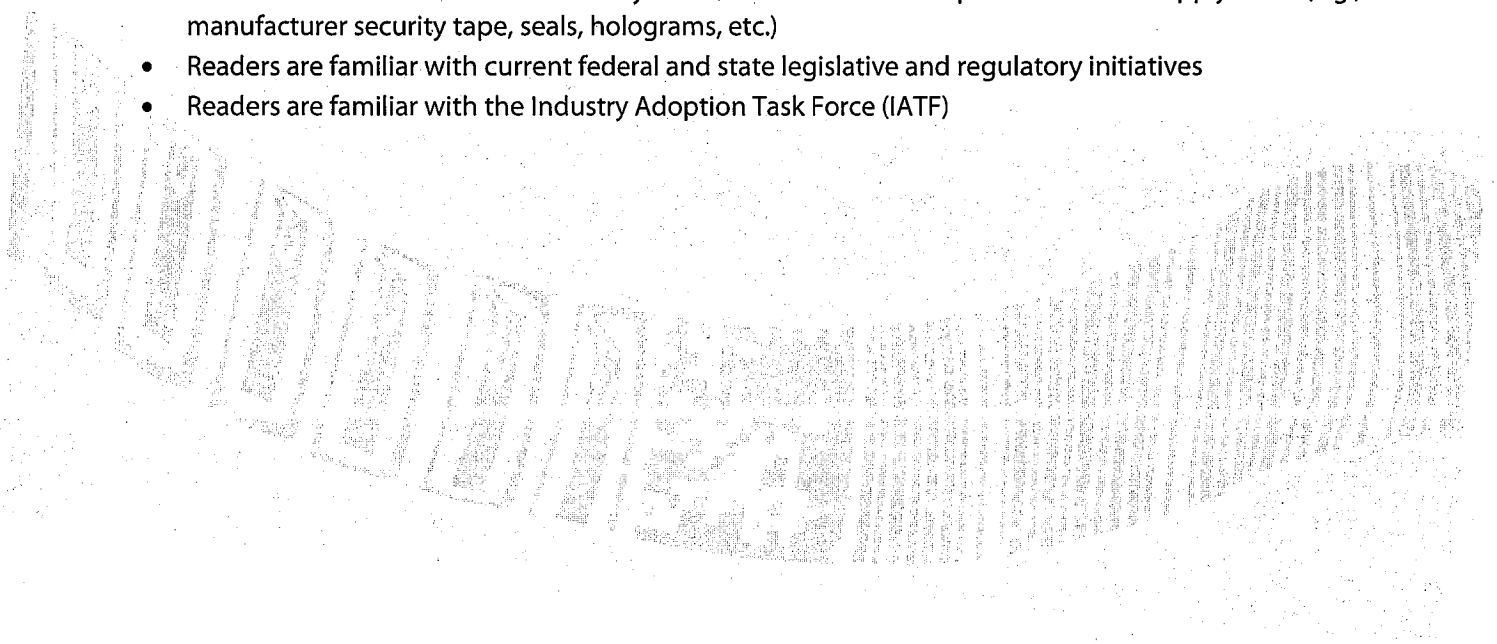
Table of Contents

Assumptions

This paper provides a general discussion on the topic of inference as it applies to the United States pharmaceutical industry. Suggestions presented in these materials are designed to provide a starting point for industry collaboration toward common solutions. They are not to be considered legal advice and are not intended to be a substitute for competent legal counsel. It is up to individual companies to comply with current U. S. state and federal regulations, and supply chain participants should rely on their own company's legal counsel for legal interpretations of statutory and regulatory requirements.

These materials have been prepared based on the following assumptions:

- Readers are familiar with U.S. pharmaceutical supply chain practices
- Readers are familiar with overt security measures used in the U.S. pharmaceutical supply chain (e.g., manufacturer security tape, seals, holograms, etc.)
- Readers are familiar with current federal and state legislative and regulatory initiatives
- Readers are familiar with the Industry Adoption Task Force (IATF)



GS1 Healthcare US would like to thank the members of the Traceability Adoption Workgroup for their hard work and dedication in developing these materials.

About GS1®

About GS1®

GS1 is a neutral, not-for-profit organization dedicated to the design and implementation of global standards and solutions to improve the efficiency and visibility in supply chains. GS1 is driven by more than a million companies, who execute more than six billion transactions a day with the GS1 System of Standards. GS1 is truly global, with local Member Organizations in 108 countries, with the Global Office in Brussels, Belgium.

About GS1 US™

GS1 US is the Member Organization of GS1 that serves companies in the United States. As such, it is the national implementation organization of the GS1 System dedicated to the adoption and implementation of standards-based, global supply chain solutions in the United States. GS1 US currently serves over 200,000 U.S. member companies -- 16,000 of which are in healthcare.

About GS1 Healthcare

GS1 Healthcare is a global, voluntary healthcare user group developing global standards for the healthcare supply chain and advancing global harmonization. GS1 Healthcare consists of participants from all stakeholders of the healthcare supply chain: manufacturers, wholesalers & distributors, as well as hospitals and pharmacy retailers. GS1 Healthcare also maintains close contacts with regulatory agencies and trade organizations worldwide. GS1 Healthcare drives the development of GS1 Standards and solutions to meet the needs of the global healthcare industry, and promotes the effective utilization and implementation of global standards in the healthcare industry through local support initiatives like GS1 Healthcare US in the United States.

About GS1 Healthcare US®

GS1 Healthcare US is an industry group that focuses on driving the adoption and implementation of GS1 Standards in the healthcare industry in the United States to improve patient safety and supply chain efficiency. GS1 Healthcare US brings together members from all segments of the healthcare industry to address the supply chain issues that most impact healthcare in the United States. Facilitated by GS1 US, GS1 Healthcare US is one of twenty four local GS1 Healthcare user groups around the world that supports the adoption and implementation of global standards developed by GS1.

Introduction

Inference is a topic of interest for stakeholders within the pharmaceutical supply chain.

What is inference?

Inference means "to derive as a conclusion based on facts presented." It enables the supply chain partners to leverage strong business practices and relationships to meet daunting challenges which involve the verification of serialized (uniquely identified) items in shipping and receiving processes.

How is it applied in business?

Inference is common in the pharmaceutical industry today in a non-serialized context, often for safety and security reasons. It is also applied extensively within the consumer packaged goods industry.

Inference is applied as a business practice when a collection of items is moved through the supply chain in a container (e.g., pallets, cases, totes, etc). It allows the container to remain intact (un-opened) so as not to undermine tamper-evident security features. It also helps maintain cost-effective material handling.

Trading partners utilize other information such as shipping documentation, physical inspections and existing trading partner relationships as part of the inference practice today. If there is a positive correlation and the integrity of the container has not been compromised, all items within the container may be accepted as being present.

With regard to serializing primary and secondary packaging, meeting existing statutory requirements demands that the integrity of serial numbers be maintained as drug products are moved across the supply chain. As with a non-serialized product, it is essential to protect the integrity of outer packaging as the product moves through the supply chain.

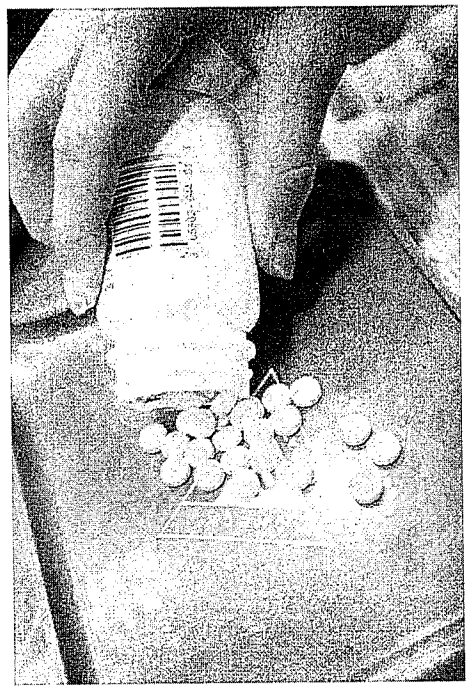
Hence, the essential topic for this document is "the practice of inference." This document and its recommendations may provide a useful starting point for other segments of the healthcare supply chain (e.g., medical devices).

The Principle of Inference

As part of the discussion, *inference* has become a topic of interest for the pharmaceutical supply chain community. *Inference* is a mechanism that enables supply chain partners to leverage strong supply chain practices to meet the potential challenges associated with the receiving/shipping of serialized items.

Inference applies in instances where a collection is moved through the supply chain in an outer container (e.g., pallets, cases, totes, etc.), and less than 100% of data carriers in that collection are read by recipients. In such circumstances, inference enables the recipient of the collection to leave the outer container intact. In order to validate receipt of the entire collection, the recipient reads the serialized identifiers for the visible items, cross-checks them with the shipping documents for the collection and outer container bundle, and verifies the integrity of the outer container bundle and its security features. If all three conditions are confirmed, the rest of the items in the collection can be inferred to be present.

Opening containers, particularly cases, as items travel through the supply chain raises serious concerns. It is not only time-consuming and costly, but it also introduces new risks. Open cases are vulnerable to tampering, theft and product mix-up. Moreover, many manufacturers today use tamper evident tape or seals to ensure the integrity of cases, and such cases remain sealed until items are staged for picking operations. Opening sealed cases would negate the effectiveness of any such security feature.



Inference can be used under the following conditions:

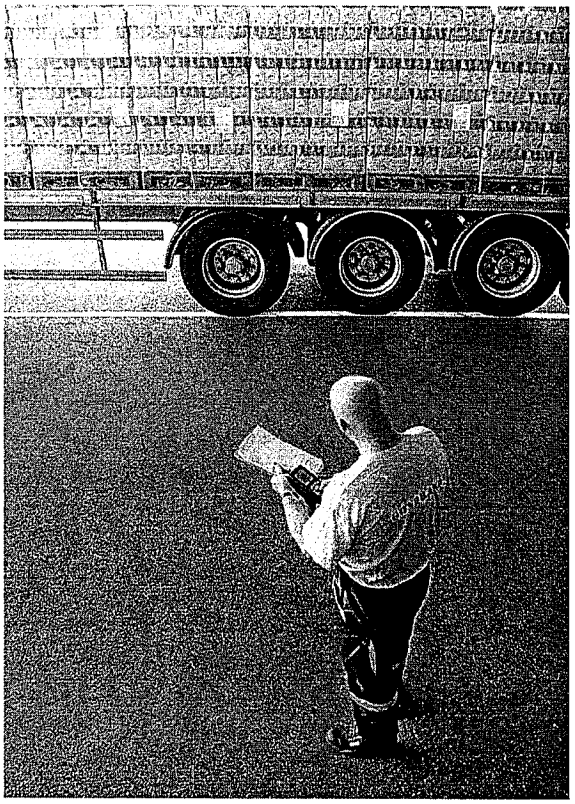
- A collection is present (e.g., case, tote, pallet, etc.).
- The collection is identified with a unique serial number, and each item in the collection is also identified with a unique serial number.
- The hierarchical relationship of all serial numbers associated with the collection ("the aggregation") is recorded as the collection is built (e.g., serial number of the pallet, serial numbers of all cases on the pallet, serial numbers of all items in each case on the pallet, etc.).
- The receiving supply chain partner receives an electronic communication detailing the aggregation of the collection (i.e., the serialized numbers and the hierarchical relationship of those serialized numbers within the collection).
- The receiving supply chain partner has assurance that the integrity of the collection has remained intact since leaving the last supply chain partner and can confirm that the integrity of the collection has not been compromised.

Inference concludes when the outer container is opened and the serialized identifier for each item in the outer container is physically available to be read.

Inference as an Applied Concept

Supply chain inference is not a new concept. In fact, it is used extensively in retail and other industries where full cases are not routinely opened at the point of receipt. Rather, the receiver uses visual inspection, supporting documentation, and existing supply chain partner relationships demonstrating shipping accuracy and integrity to validate receipts. For example, the identity of a barcoded unit that is packed in a sealed case can be inferred based on supporting evidence such as:

- No signs of tampering
- Clean bill of freight
- Delivery consistent with expectations (day, time, etc.)
- Standard case count
- Match across outer container serial number, purchase order, advance shipping notice, shipping documentation, and visual inspection
- Existing history with the supply chain partner



Inference is also commonly used in the pharmaceutical supply chain today – often for safety and security reasons. For example, many customers prefer to leave manufacturer security features like seals or tamper evident tape intact in order to decrease risk of tampering or loss. Moreover, some customers require manufacturer unopened cases to ensure package integrity. In these situations, inference is a practical necessity. The use of inference is also common for other types of packaging that are routinely left intact (e.g., bundle of 10 count syringes, etc.). In all of these examples, supply chain partners using inference would rely on their existing processes for resolution of shortages and other exceptions.

Applying Serialized Inference to Pharmaceuticals in the Supply Chain

Within the context of the U.S. pharmaceutical supply chain, *serialized inference* is defined as the process a supply chain partner could use to facilitate safety and efficiency in the receiving of items without physically reading each serialized identifier at the time of receipt. The identity of serialized items can be inferred based on information provided by the up-stream supply chain, reasonable inspection of the product, and application of *Serialized Inference Processes* by both the shipping and receiving partners. *Serialized Inference Processes* define the specific actions that should be completed within aggregation, shipping and receiving processes in order to support the use of inference in the supply chain. In order to use inference for pharmaceuticals and pedigree, *Serialized Inference Processes* should be defined for each packaging unit (e.g., pallet, case, tote, etc.) for all aggregation, shipping and receiving processes.

For example, Table 1 presents *Serialized Inference Processes* that detail the steps recommended for inclusion in aggregation processes in order to facilitate the use of inference:

Table 1: Serialized Inference Processes for Aggregation Processes

Single item commission	Apply serial number to one single Item. (Note: all items are associated with a lot.)
Item to case aggregation	Apply serial number to case and build item-to-case hierarchy.
Case to pallet aggregation	Apply serial number to a homogenous pallet comprised of cases of all one product, and build case-to-pallet hierarchy. *(May be a full pallet or a partial pallet.)*
Tote, mixed case or overpack aggregation	Apply serial number to case, tote or overpack containing either a mixture of SKU's or one or more items of a single SKU, and build item-to-case hierarchy. For overpacks, this may result in multiple levels of hierarchy to be inferred depending on product form. *(Typically conducted as part of a pick/pack/ship operation.)*
Mixed pallet aggregation	Apply serial number to pallet of mixed cases or totes, and build case-to-pallet or tote-to-pallet hierarchy. *(Pallet could contain mixed cases and/or full cases. The full cases could be from one product or from multiple products.)*

In contrast to the *Serialized Inference Processes* for aggregation shown above that deal primarily with tagging and information collection, *Serialized Inference Processes* for shipments and receipts deal primarily with reading and inferring tags and identifiers. It should be noted that *Serialized Inference Processes* for shipments and receipts assume the hierarchy and packaging integrity remain intact from the Commission/Aggregation process.

Inference in Action in the Pharmaceutical Supply Chain

Using the *Serialized Inference Processes* described above, supply chain partners can use inference as a method for ensuring that there is enough evidence to certify receipt of serialized items without physically reading each unique identifier. The inference process from manufacturer to wholesaler to pharmacy is demonstrated below in a chain of custody model representing the shipping and receiving of a manufacturer sealed case of pharmaceuticals.

! The following example is intended for use with homogeneous cases, but does not preclude the use of inference in other situations. The example also does not cover exception processing.

Rationale for Inference:

The case remains in the control of the company.

Product movement practices are documented and used (for example, a company's own processes, Good Manufacturing Practices (GMP), good distribution practices, etc.).

The site is physically secure.

The case is visually intact.

The previously gathered information from product movements are retained.

Manufacturer

Step 1. All identifiers of bottles are scanned as they are packed into a case. (In the case of RFID, the items may be scanned or read after they are packed.)

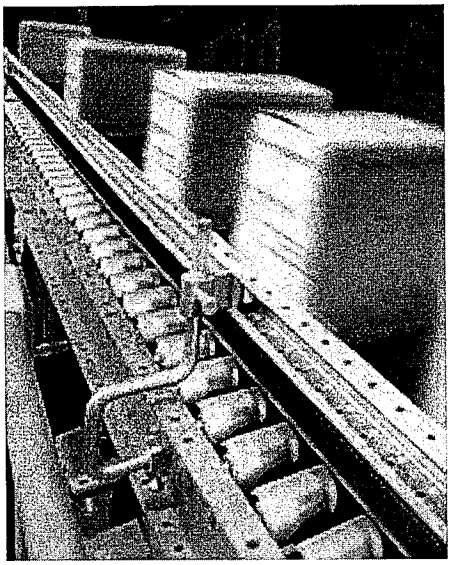
Step 2. A case identifier is created and scanned, and the case/bottle identifiers are associated with one another within the manufacturer's system.

Step 3. The case is put away.

Step 4. Upon shipping the case to a supply chain partner, the manufacturer "infers" that the previously identified bottles are in the case, and creates the appropriate electronic shipping documents based on that information.

Step 5. Electronic shipping documents are sent to the wholesaler.

Wholesaler



Step 1. The wholesaler receives the electronic shipping documents.

Step 2. The product arrives at the wholesaler.

Step 3. The wholesaler visually confirms the integrity of the shipped case or pallet.

Step 4. Product is inferred based on electronic shipping documents that match the shipped case or pallet, security features and integrity of the container are intact.

Step 5. The case is put away.

Step 6. When shipping the full sealed case to a supply chain partner, the wholesaler "infers" that the packages identified in the manufacturer's shipping documents are in the case, and creates the appropriate electronic shipping documents based on that information.

Step 7. The wholesaler's electronic shipping documents are sent to the pharmacy distribution center.

Pharmacy Distribution Center

Step 1. The pharmacy distribution center receives the electronic shipping documents.

Step 2. The product arrives at the pharmacy distribution center.

Step 3. The pharmacy distribution center visually confirms the integrity of the shipped case or pallet.

Step 4. Product is inferred at the point of receipt based on electronic shipping documents that match the shipped case or pallet.

Step 5. The case is put away.

Step 6. The case is opened for picking.

Step 7. Items are picked from the case, read and matched against the wholesaler electronic shipping documentation effectively concluding inference.

Step 8. The pharmacy distribution center creates and sends shipping documents to the pharmacy.

Pharmacy (wholesaler ships direct to pharmacy)

Step 1. The pharmacy receives the electronic shipping documents.

Step 2. The product arrives at the pharmacy.

Step 3. The pharmacy visually confirms the integrity of the shipped case or pallet.

Step 4. Product is inferred at the point of receipt based on electronic shipping documents that match the shipped case.

Step 5. The case is put away.

Step 6. The case is opened for stocking.

Step 7. Inference can conclude when the case is opened and the serialized identifier for each item in the case are physically available to be read.

The Decision to Use Inference

The use of inference remains an individual company decision. In deciding whether to use inference for items moving through the supply chain and/or internal processes, a company will build an internal case for inference that can be thought of as building layers of trust. Each layer reinforces confidence in the use of inference, and strengthens the case that items for which receipt was inferred were actually received.

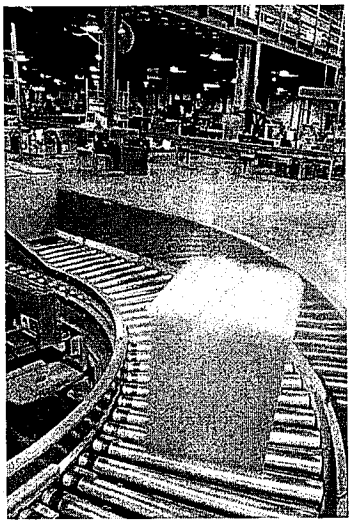
There are four factors that can be considered when deciding whether to use inference: Trusted Relationships; Best Practices; Corroborative Information; and Physical Security. Some of the qualifications to be considered for each factor are presented below. These can be used when building the case for a company's decision to use inference.

Supply Chain Partner Relationships

The relationship between supply chain partners can impact the decision about whether to use inference to a great degree. The level of trust in supply chain partner relationships can be established using a number of indicators including:

- Agreements
- Audit results
- Documented practices of the supply chain partner
- Past performance as measured by the historical accuracy of received documentation (e.g., advance ship notice, pedigree, bills of lading, etc.), shipment condition (e.g., intact, sealed cases) and accuracy of received bundles

Best Practices



Good business practices, both a company's and its supply chain partners, contribute to a secure supply chain (e.g., good manufacturing practices; good distribution practices; good pharmacy practices; etc.). The level of trust in business practices can be established using a number of indicators like:

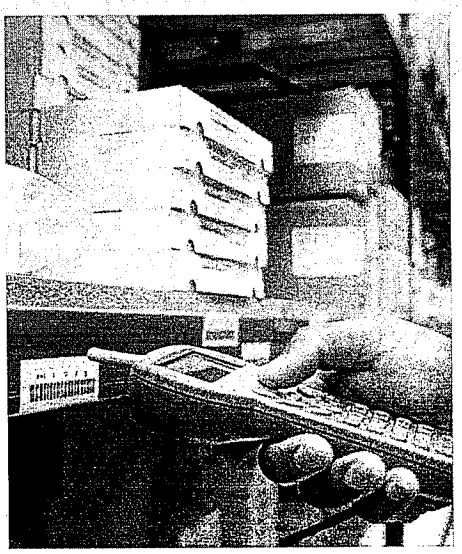
- Supply Chain Partner Score Carding
- Performance Auditing Process
- Documented controls and Standard Operating Procedures
- Routine capture of quality metrics to minimize "defects" of inbound and outbound product
- Implementation of process changes whenever process errors are detected in order to prevent future errors
- Periodic review of processes for improvement opportunities

In addition, when a company uses inference practices, its supply chain partners may require additional documentation, assurances about the use of best practices, and/or proof of physical security.

Corroborative Information:

Documentation and observations for the particular items under consideration also inform a decision about whether inference would be appropriate. Various types and sources of corroborative information can be used, including:

- Physical inspection showing:
  - Original manufacturer tape intact
  - No signs of tampering
  - Clean bill of freight
  - Complete pedigree trail
  - Confirmation of outer packaging identification against supporting documentation
- Transit time consistent with expectations
- Authentication capability (i.e., direct supply chain partner verification, repositories or services where supply chain partners can verify serial numbers)
- Electronic documents such as:
  - EPCIS ship and receive information
  - Pedigrees
  - Advance Ship Notices
  - Bills of Lading

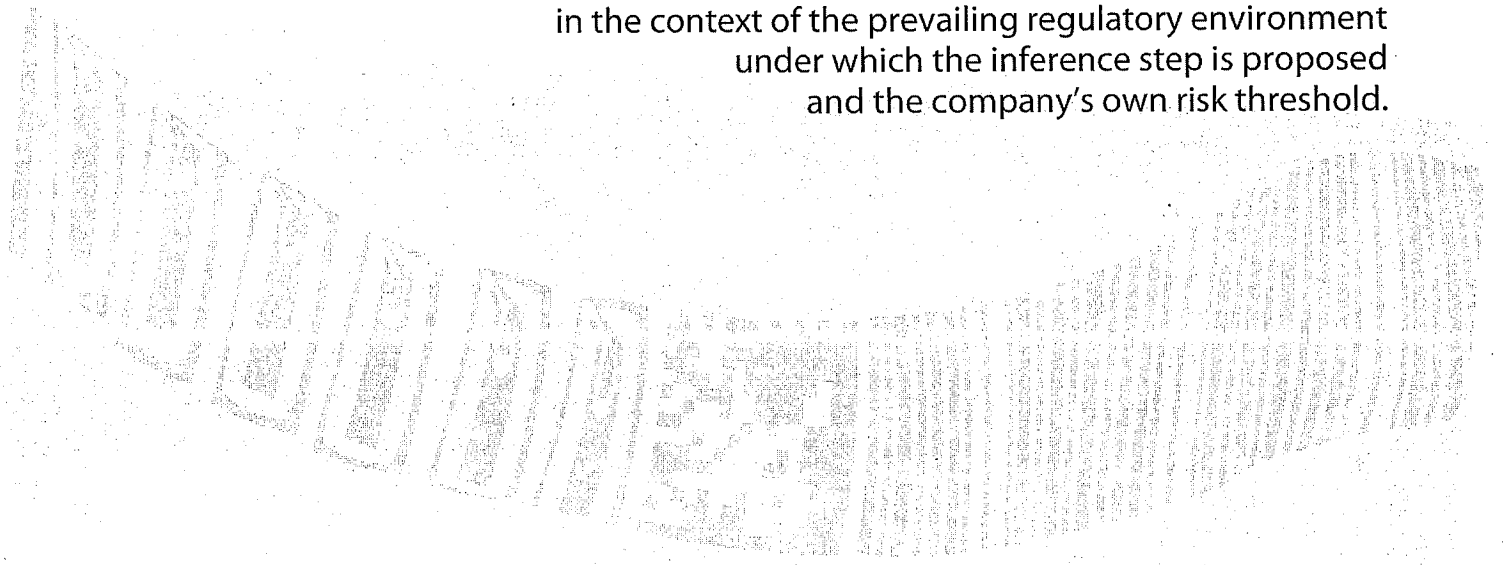


Physical Security

Documented security policies and procedures within physical plants, distribution centers and facilities contribute to establishing the trust to support the decision to use inference. Likewise, documented security policies and procedures for transport vehicles are an important consideration as well.

The practice of inferring the contents of packaging based on secure corroborative information, best practices, trusted supply chain partner relationships and physical security is thought to be an appropriate means to provide the appropriate level of security and efficiency within the supply chain.

Ultimately, each company must consider all of this information in the context of the prevailing regulatory environment under which the inference step is proposed and the company's own risk threshold.



Appendix: References & Recommended Reading

- GS1 Healthcare US Website

  http://www.gs1us.org/healthcare

- GS1 Healthcare US Document Library

  http://www.gs1us.org/hclibrary

- Industry Announcements

  http://www.gs1us.org/library?EntryId=344

- GS1 Healthcare US Web Seminars

  http://www.gs1us.org/hcedu

- GS1 US Glossary

  http://www.gs1us.org/glossary

- GS1 US Product Catalog

  GS1 US offers a comprehensive line of technical implementation guidelines for GS1 Standards.

  http://www.gs1us.org/productcatalog

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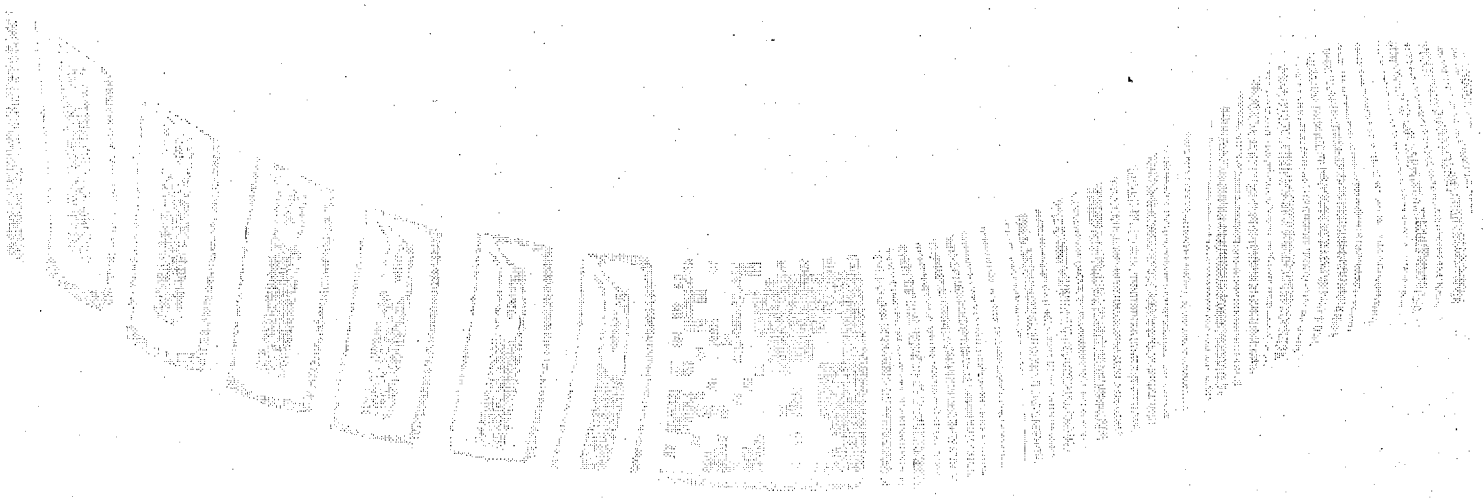

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GS1 Healthcare® US

Pilot **Report**

Lessons Learned About Serialization

Using GS1 Standards

Experiences of a Pharmaceutical Manufacturer

Profile of the Supply Chain Member

Large, multi-national manufacturer of pharmaceuticals and medical devices.

Background

The question of how to manage the transition to serialization is an important one for the U.S. pharmaceutical industry. Manufacturers will likely use a well-choreographed conversion process to implement serialization across the numerous SKUs in their product line over time. Simultaneously, demand-side partners will be choreographing their own transition to serialization. Transitions on both sides suggest a complex operating environment in which manufacturers will be managing production and processing orders for both serialized and non-serialized products at the same time.

In preparation, this manufacturer wanted to learn more about serialization in terms of tagging and aggregation. In addition, they wanted to gain insight about the challenges involved in managing and processing inventories that contain both serialized and non-serialized products, and about interacting with trading partners in that environment.

Program Overview

The pilot program was conducted in three phases. The goal of Phase 1 was to get the serial number engine in place in the company's serial number management infrastructure. Because this was a significant undertaking in terms of both time and money, the company decided to minimize the operational effort in Phase 1 by limiting serialization to the case and pallet level only. The goal of Phase 2 was to extend serialization to the item level and get real world experience with item-level RFID. The goal of Phase 3 was to implement item-level serialization and case aggregation on the production line.

Two high-volume products were selected for the pilot program. Product A was a solid-dose pharmaceutical packaged in square bottles. Product A was used for Phase 1 and Phase 2 of the pilot. Product B was a biologic packaged as a two-pack. Product B was used for Phase 3 of the pilot. Throughout all phases of the pilot, individual units and cases were identified using GS1 GTINs plus Serial Number, and pallets were identified using GS1 SSCCs.

GS1 Standards Used

GS1 Identifiers

Item: **Serialized Global Trade Item Number® (GTIN®+ serial#)**
Case: **Serialized Global Trade Item Number (GTIN + serial#)**
Pallet: **Serial Shipping Container Code (SSCC)**

GS1 Data Carriers

Item: **GS1 DataMatrix (2D Barcode)**
GS1 EPC/RFID Tag (UHF Gen2)
Case: **GS1-128 Barcode**
GS1 EPC/RFID Tag (UHF Gen2)
Pallet: **GS1-128 Barcode**
GS1 EPC/RFID Tag (UHF Gen2)

Phase 1

Case & Pallet Serialization ◆ EPC/RFID & Barcode ◆ Product A

Phase 1 began in 2007 and lasted approximately nine weeks. Most of the effort took place at the company's distribution center. During this phase, the serial number engine was deployed as part of the company's global IT infrastructure. Serialized identifiers were assigned to cases and pallets, and encoded into GS1-128 barcodes and EPC/RFID tags that were then applied to cases and pallets. Serialized cases of Product A were then aggregated into serialized pallets. (There were no mixed cases.) Both a conveyor and AI Mobile Handheld Units were used to read the tags during the aggregation process. Upon shipment, the serialized information was integrated into ASNs.

The company enlisted one of its top distributors for the Phase 1 pilot. The pilot included 9 weekly shipments to the distributor, with a different scenario executed each week (e.g., missing case label; unreadable case label; missing pallet label; unreadable pallet label; more/less cases aggregated to a pallet than usual; pallet mismatch; etc.). Upon receipt, the distributor attempted to read each case and pallet RFID tag. Then, the distributor compared the serialized shipments to the serialized ASNs, and provided manual confirmation of the results back to the company via email. Over 3100 cases were shipped in Phase 1.

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Phase 2

Item/Case/Pallet Serialization ♦EPC/RFID & Barcode ♦ Product A

The goal of Phase 2 was to build on Phase 1 by extending serialization to the item level for Product A and gain insight into item-level RFID. Items were marked with 2D barcodes and EPC/RFID tags that were pre-encoded at the label vendor. Cases and pallets were marked with GS1-128 barcodes and EPC/RFID tags. During Phase 2, the pilot included cases of varying quantities. The company considered this their first step toward understanding the management of mixed cases (i.e., cases with mixed products).

Most of Phase 2 took place at the company's manufacturing center. However, access to the live production line was severely restricted. Therefore, the company chose not to aggregate cases on the production line in Phase 2. Instead, there was a separate RFID reader station situated near the production line. That station was used to aggregate cases, validate the number of reads, and commission/encode tags for the cases. When pallets were built for an order, the user would scan each case to be placed on the pallet. During delivery packing, a conveyor system read the case barcode, case EPC/RFID tag, and item EPC/RFID tag. During pallet packing, a handheld scanner was used to scan the pallet barcode.

The serialized identifiers were integrated into the ASN and a draft pedigree document. The company enlisted its top three distributors for Phase 2. The distributors received and compared the serialized shipments to the serialized ASNs and pedigrees, and provided manual confirmation of the results back to the company via email. (NOTE: The entire aggregation hierarchy was not verified by any trading partner.)

Phase 2 began in 2008 and lasted approximately one year. The first six months was dedicated to designing, developing, building, testing, and implementing the system. For the rest of the year, 2-3 serialized orders were shipped per week.

Phase 3

Item/Case/Pallet Serialization ♦ Barcode ♦ Product B

The goal of Phase 3 was to fully enable serialization for a manufacturing line and one area in the distribution center (i.e., implement the "go live" design for item-level serialization. For Phase 3, the company used Product B, the biologic. Therefore, there was no RFID due to FDA pilot guidance. 2D barcodes were pre-encoded with GTIN + serial number at the label vendor, and applied to Product B on the production line. Cases and pallets were marked with GS1-128 barcodes, and the serialized aggregations were integrated into ASNs. Once again, the company enlisted several top distributors for Phase 3, including a distributor who had pharmacy outlets so that the company could test a few transactions further down the supply chain.

Phase 3 began in 2009 and is technically still continuing with periodic shipments of serialized products. (NOTE: Document model pedigrees were discontinued.)

Cross-Functional Team

The company formed a large, cross-functional team for the pilot program with expertise across key business and operational areas. The team included members from the business group (who owned the funding), packaging engineering (who took the lead on labels and RFID), and engineering (who supported plans and came up with new technologies for the plant). In addition, the team included members from the manufacturing plant and the distribution center, including representatives from business, operations and quality control. There were also team members from divisional and corporate IT to support hardware, software, infrastructure and integration needs throughout the program.

Systems

The pilot program touched numerous systems across manufacturing and distribution, including:

- PLC (Programmable Logic Controller)
- HMI (Human to Machine Interface)
- Edge Systems
- Manufacturing Middleware
- Serial Number Management Infrastructure
- EPCIS
- ERP (Equipment and Resource Planning)
- EDI

Metrics

There were many metrics defined for the pilot at the beginning and measured throughout the pilot program. Some of those metrics are listed below:

Manufacturer:

- Item RFID read rate (during packaging)
- Item RFID read rates (during distribution using conveyor)
- Item 2D barcode read rate
- Case label reject rate
- Pallet label reject rate
- Item to case aggregation exceptions
- Case to pallet aggregation exceptions
- Item/case/pallet aggregation accuracy
- Duplicate serial number exceptions
- Time to serialize 1 lot
- Average time to process a pallet shipment
- Time for item to case aggregation (barcode and RFID)
- Time for case to pallet aggregation (barcode and RFID)
- Time for case to pallet disaggregation (barcode and RFID)
- Serialized ASN exceptions
- Pedigree creation/processing/signing exceptions
- Integration exceptions between serialization infrastructure and EDI
- Integration exceptions between EDI and RFxcel

Trading Partners/Distributors:

- Item RFID read rates at trading partner (conveyor only)
- Case RFID read rates at trading partner (conveyor + portal)
- Pallet RFID read rates at trading partner (portal reads)
- Pedigree and physical product match success rates

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Ultimately, the team felt that there were too many metrics, and shares the following lesson: beware of defining too many goals and metrics for the pilot at the beginning because you do not know enough at that point to understand what are *achievable* goals and *valuable* metrics.

Pilot Experience

At the beginning, the company brought in a leading consulting company to do a long range plan and manage Phase 1 and part of Phase 2. Other vendor support was brought in as well. Even though the company believes the additional support was necessary for the program, it became clear that many vendors did not know any more than the project team.

The team found that the pilot experience was really driven by the business side, right down to the selection of products and the production lines. Moreover, production constraints had a significant impact on the pilot (e.g., schedules; revenue; production needs; etc.). Even as learning continues and process improvements are identified, it remains very difficult to get time on the line to make the improvements, especially with high revenue products and highly utilized lines.

Although a pilot is developed in the positive case, the company found that the pilot experience is very valuable for learning what to do when something goes wrong [i.e., learning how to develop system(s), people and processes to respond]. The pilot began with company's interest in learning more about how to work with serialized products. In the end, the company believes the pilot program definitely helped them to move forward in this area.

Lessons Learned

Project Management

- **The project plan needs to account for manufacturing line charges for pilot activities.**
- **Plan to have labels in-hand early in the project schedule to avoid delays.**
  - Delivery lead-time for a large quantity of RFID labels was greatly underestimated by the label vendor because of the market demand for tags and the labor required for processing/encoding.
- **Frequent meetings (approximately every other day) with the project team at the plant two weeks prior to and during the implementation and go live phases proved very valuable.**
  - Plans were solidified.
  - Many minor but necessary actions were identified and resolved.

Vendors

- **Evaluating vendors is very important. Learning how to evaluate them is an ongoing process in which you get better at knowing what questions to ask them.**
  - For example, aggregation accuracy is a big issue. If vendors do not bring it up themselves, especially in terms of pricing (i.e., price goes up depending on how accurate aggregations need to be), it may signal lack of experience.
- **Confirm a vendor's knowledge of industry and safety standards.**
- **Understand vendor weaknesses (e.g., ability to scale; staffing; support; familiarity with standards; experience with RFID; etc.).**
- **Negotiate well and add contractual provisions wherever possible.**
  - Vendor contracts and project accountability should be agreed to before selecting a vendor.
- **Dedicate a project management resource to each external vendor to properly manage delivery.**
- **Having two different vendors collaborate on the software requirements, design and implementation of a solution did not work well.**
  - It is preferable for one vendor own the total solution.

Labels & Tagging

- **The RFID tag embedded in a label can cause smearing when the barcode is printed on top of it.**
- **Production line rollers that apply labels to bottles may need to be changed so that they do not damage or crush the RFID tag.**
- **The labeling process should verify an RFID tag *before* and *after* its application to the bottle.**
- **2D barcodes should be separated from other barcodes on the label so that scanning is more efficient and accurate.**
  - When scanning with the handheld, operators had to cover the linear barcode with their finger so it would not be read.
- **The 2D data matrix barcode proved to be very robust (no failures).**
- **Case-level RFID labels proved to be very reliable (99.x% read rates).**

RFID

- **Metal acts as an unintentional antenna/signal reflector which can result in stray reads. Avoid metal near RFID readers.**
  - Assess all metal surfaces in production and distribution areas (e.g., tables, shielding, conveyors, etc.) so that RFID readers are not negatively affected.
  - Grounding metal objects helps, but not significantly.
  - Can also try adjusting the antenna tuning and/or using RF blocking material.

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- **RFID tag readability can vary depending on the reader equipment used.**
- **Using handheld readers to scan RFID tags did not work well. It took a long time to read the tags, and the tag had to be physically separated from all other RFID-labeled products to avoid stray reads.**
- **RFID read rates are not 100%.**
  - Use it wisely and establish reasonable expectations.
  - Come to an understanding of what constitutes "quality performance."
  - Avoid "100% or nothing" metrics for success on read rates.
  - Back-up barcodes are recommended.
- **Although there are issues with RFID, it is a progression. The technology and the knowledge base are growing.**
- **Tag orientation made a big difference in read time.**
  - When the tags were facing the antenna, reads were instantaneous.
  - In contrast, conveyor reads in the distribution center (DC) were not consistent because tags were facing forward on the conveyor and the antennas were on the side.
  - Address issues by adjusting antenna placement and/or tuning the reader.
- **Equipment and packaging design needs to be in sync with respect to RFID tag orientation (and potentially barcode placement) for both manufacturing and DC equipment.**
  - Need end-to-end packaging and equipment designs that consider tags/barcodes, readers, antennas, tuning and tag orientation.

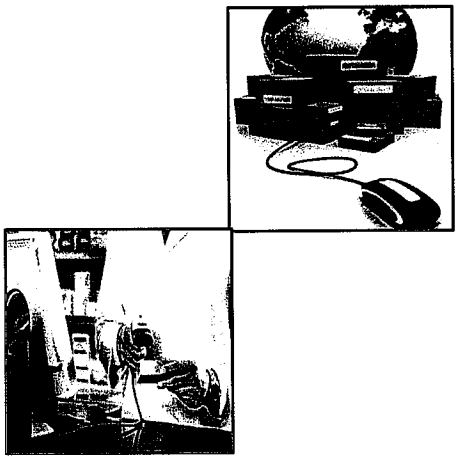
Hardware

- **A physical keyboard was preferred over a touch screen keyboard.**
  - The virtual keyboard is difficult to use and slows down the process.
- **Use a fixed barcode scanner on the conveyor that can read *across the conveyor*.**
- **Electrical variations in the DC affect the performance of the conveyor.**
- **Conveyor solutions need rigorous functional and stress testing to ensure the interface between the application and PLC (Programmable Logic Controller) is robust.**
- **Handhelds and portals (as opposed to a conveyor) may be a better solution when using 2D barcodes as the item-level data carrier.**
- **The serial number label printer encountered out-of-sync conditions during label reload causing aggregation errors.**
  - When the roller ran out of labels, the system buffered the current label and paused to wait for labels to be loaded. However, the label in the buffer was not purged once the printer was reloaded and the system was refreshed. As a result, the buffered label printed again, causing an out-of-sync condition where everything was off by 1 and all of the aggregations were off.
  - QA system only checked that the label *printed properly*, not whether it was *correct* per the numbering system.
  - Not obvious to catch and can go unnoticed, causing a lot of re-work.

Business Processes

- **Adding serialized barcodes to cases in addition to the normal barcode made it difficult for the staff to know which barcode to scan.**
  - Caused confusion.
  - Training and clear instructions are needed.
- **Disaggregating units from a case (or cases from a pallet) before aggregating to a shipment is inefficient.**
  - Manual rework / aggregation is extremely labor intensive and error-prone.
  - Need a process that supports scanning once to perform both functions.
- **Discrepancies (i.e., shortages or overages) reported by trading partners can be investigated using RFID tag read results.**
  - Example: comparison of tags read in the manufacturer's DC to tags read at the trading partner's DC proved that some of the items that were claimed to be short were actually sent and received.
- **Receiving a separate, RFID-specific PO was critical to the ordering process for the pilot. But, this is not practical for the production environment and will need to be addressed in the future.**

For more information and additional resources about 2015 Readiness available from GS1 Healthcare US (including guidelines, workshops and pilots), visit *www.gs1us.org/2015ready*



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The Pharmaceutical Supply Chain: Improved Security through Statistical Sampling

By Barchi Gillai, Ph.D.

June, 2012

STANFORD
GRADUATE SCHOOL OF BUSINESS
Global Supply Chain
Management Forum

Executive Summary

A relatively comprehensive system of laws, regulations, and enforcement by Federal and State authorities has kept the incidence of drug counterfeiting in the United States low. Still, for over a decade, the FDA has seen growing evidence of efforts around the world by increasingly well-organized counterfeiters backed by sophisticated technologies and criminal operations to profit from drug counterfeiting.

In response, the FDA developed a comprehensive framework for securing the pharmaceutical supply chain against modern counterfeit threats. Among other things, the FDA has encouraged the use of electronic track and trace technologies and electronic pedigrees, as well as product authentication technologies. These recommendations were translated into state legislation in California, where e-pedigree requirements for prescription drugs will take effect starting in 2015.

Item level serialization and track and trace activities can no doubt help reduce the risk of counterfeit items being introduced into the pharmaceutical supply chain. At the same time, there are also advantages to keeping outer containers closed as long as possible, as open cases are vulnerable to tampering, theft and product mix-up. These security concerns are one of the drivers behind the practice of inference, under which companies use other evidence, rather than opening outer containers and scanning each individual item, in order to verify the integrity of a shipment. While inference is common in the pharmaceutical industry, its use remains an individual company decision, and is usually used only when there is strong indication that the integrity of shipments has not been compromised.

Nevertheless, the practice of inference is not risk-free, and may provide an opportunity – even if only a small one – for counterfeit products to be introduced into the supply chain. To address this concern, the study described in this report focused on developing a statistical sampling model, to be used by companies throughout the pharmaceutical supply chain. Using statistical sampling on a regular basis, and in combination with other good practices related to inference, would allow companies to continue using inference and maintain most of the benefits associated with this practice, while at the same time limiting the risks associated with inference and increasing confidence in the security of the supply chain.

The statistical sampling model developed in this study was adopted from the international standard ABC-STD-105 (also known as MIL-STD-105D, ANSI/ASQC Z1.4, and ISO 2859). It is based on the concept of an Acceptable Quality Level (AQL), which is defined as the percent nonconforming that, *for acceptance sampling purposes only*, is considered acceptable as a process average. The model allows users to determine for each incoming shipment the required

sample size and acceptance number (maximum number of nonconforming items allowed) based on the shipment size and selected AQL.

The statistical sampling model always uses two types of inspections, namely *normal* and *tightened*. Normal inspection is selected in the absence of unsatisfactory quality history, while tightened inspection, which is based on more stringent acceptance criteria, must be used whenever the quality history is unsatisfactory, unknown, or when there are other good reasons for being suspicious about quality. Companies may also choose to use *reduced inspection* in addition. The acceptance criteria under reduced inspection are less stringent compared to normal inspection, and it is therefore recommended that companies be cautious about using this type of inspection and allow it only when they feel confident that the high quality level of incoming shipments is likely to continue.

When using the sampling model, one should make a clear distinction between true counterfeits identified, and nonconformities that are related to incomplete or inaccurate product pedigree. In the case of a true counterfeit, the receiving party should take *immediate steps* to address the issue based on the company's internal policy. Only when other types of nonconformities are identified should the instructions specified in the sampling plan be followed.

In addition to this report, which explains in detail the characteristics of the sampling model, how it was constructed and how it should be used, we also developed an Excel® model, which allows users to determine the specific sampling plan for each incoming shipment. In addition, the model displays key quality characteristics, which demonstrate the overall impact of the selected sampling plan on the expected quality level of incoming shipments after inspection. The Excel model also calculates the average total inspection rate associated with each sampling plan, which provides an indication to the direct cost associated with the plan.

While using the statistical sampling model, it is important to keep in mind that the model only ensures that *in the long run* the average outgoing quality will be close in value to the chosen AQL. When shipments are isolated or infrequent, a sampling plan based on a desired AQL value may not give the receiving party a sufficient level of protection. In those cases, it will be better to either conduct 100% screening of the entire shipment or select a sampling plan based on the overall level of protection it provides as can be seen from its Operating Characteristic curve.

It is important to keep in mind that by definition, no sampling plan can ensure the acceptance of only perfect shipments. As an alternative, the summary of this report briefly discusses the option of tagging products with item-level RFID, which allows automatic scanning of all items in a shipment while avoiding the need to open up sealed cases to scan products' ID.

Introduction

In the United States, a relatively comprehensive system of laws, regulations, and enforcement by Federal and State authorities has kept the incidence of drug counterfeiting low, so that Americans can have a high degree of confidence in the drugs they obtain through legal channels. For over a decade, however, the FDA has seen growing evidence of efforts around the world by increasingly well-organized counterfeiters backed by sophisticated technologies and criminal operations to profit from drug counterfeiting[1].

To respond to this emerging threat, the FDA formed a Counterfeit Drug Task Force in July 2003. This group received extensive input from numerous resources on a very broad range of ideas for deterring counterfeiters. Based on these inputs, the FDA developed a comprehensive framework for securing the pharmaceutical supply chain against modern counterfeit threats. Among other things, the task force encouraged the use of electronic track and trace technologies and electronic pedigrees[2], as well as product authentication technologies. Under California state legislation, e-pedigree requirements for prescription drugs will take effect on a staggered basis from January 1, 2015 through July 1, 2017[3]. A national requirement by the FDA may follow[4].

While item level serialization and electronic product pedigree certainly help secure the supply chain, there are also advantages to keeping outer containers closed throughout the supply chain and avoid opening them too soon before they reach their final destination. Open cases are vulnerable to tampering, theft and product mix-up. Moreover, many manufacturers today use tamper evident tape or seals to ensure the integrity of cases, and such cases remain sealed until items are staged for picking operations. Opening sealed cases negates the effectiveness of any such security feature.

These security concerns are one of the drivers behind the practice of inference[5], which is common in the pharmaceutical industry. From a business perspective, inference also helps products to move faster along the supply chain, and helps maintain cost-effective material handling. The use of inference remains an individual company decision. Usually, companies will use inference only when there is strong indication that the integrity of each shipment has not

[1] Source: http://www.fda.gov/Drugs/DrugSafety/ucm169825.htm

[2] A drug's pedigree represents the complete history of a given product's chain of custody from the manufacturer to the point of dispensing. With electronic pedigrees, the data collection as well as the management of product pedigrees is done electronically.

[3] Source: http://www.pharmacy.ca.gov/about/e_pedigree_laws.shtml

[4] Source: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086119/

[5] Inference applies in instances where a group of items (e.g. bottles of medication) move through the supply chain in an outer container (e.g. a case, tote, etc.). Rather than opening the outer container to verify that all individual items are present, other evidence is used in order to verify the integrity of the shipment.

been compromised. The factors impacting such a decision may include the level of trust between the business partners, the degree of good business practices in use by the company and its supply chain partners, the availability of complete documentation of the shipment, physical inspection which shows no signs of tampering, and documented security policies in use by the company and its supply chain partners.

Nevertheless, the practice of inference is not risk-free, and may provide an opportunity – even if only a small one – for nefarious characters to introduce counterfeit products into the supply chain. To address this concern, the study described in this report focused on developing a statistical sampling model, to be used by companies throughout the pharmaceutical supply chain. The model allows users to determine, for any given shipment, the sample plan (sample size and acceptance criteria) that in the long run will reduce the risk of a security breach to a sufficiently low level. Using statistical sampling on a regular basis, and in combination with other good practices related to inference, would allow companies to continue using inference and maintain most of the benefits associated with this practice, while at the same time limiting its associated risks and increasing confidence in the security of the supply chain.

The remainder of the report provides a brief overview of the structure of the pharmaceutical supply chain, followed by a short discussion of the practice of inference. We then discuss at a high level the concept of statistical sampling, followed by a detailed discussion of the statistical sampling model developed in this study, how it was constructed and how it should be used. We conclude the report with a brief summary and future recommendations.

The Pharmaceutical Supply Chain

This study looks at the pharmaceutical supply chain, with a specific focus on forward logistics of solid oral medication (tablets), which are packed in bottles or cartons[6]. There can be a number of supply chain structures and packaging practices for this product category, as described below. The proposed sampling model is applicable under all these scenarios.

Single Wholesaler

Under this scenario, the products are delivered from the manufacturer to a wholesaler and from there to independent pharmacies (see Figure 1). The manufacturer will most likely ship multiple cases or pallets of a single type of product to the wholesaler. As the quantities shipped

[6] For convenience, throughout the report individual items are referred to as “bottles”, even though the tablets of medication can be packed in other types of individual packaging, such as cartons.

to individual pharmacies are much smaller, the wholesaler will likely open up the cases received from the manufacturer, and ship individual bottles to the pharmacy in totes.

Figure 1: Supply Chain Involving a Single Wholesaler

Large and Secondary Wholesalers

Under this scenario, the products are shipped from the manufacturer to a large wholesaler who, in turn, ships smaller quantities of the product to a secondary wholesaler (See Figure 2). Independent pharmacies will place their orders with the smaller wholesaler.

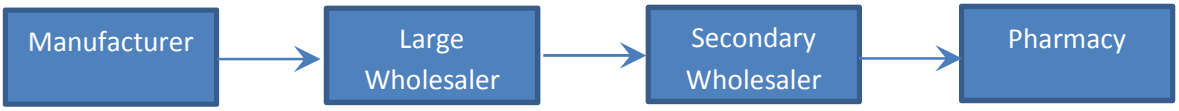

Figure 2: Supply Chain Involving Large and Secondary Wholesalers

Drop Shipments

Under this scenario, the manufacturer is the one to fulfill a pharmacy's order, in case the wholesaler the pharmacy placed the order with does not have the ordered items in stock (see Figure 3). The wholesaler will be the one to request the manufacturer to drop ship the products directly to the pharmacy.

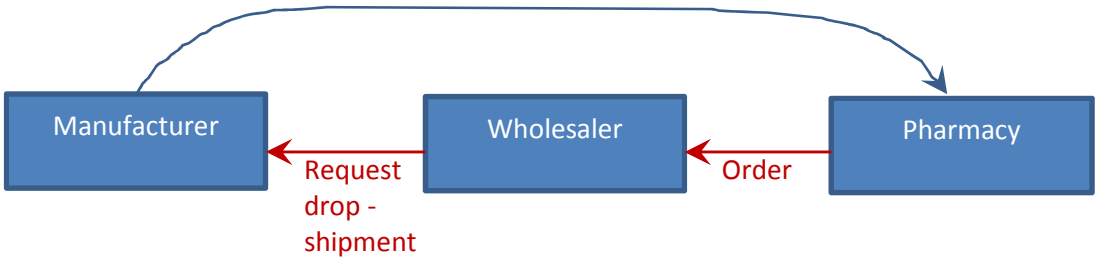

Figure 3: Supply Chain Involving Drop Shipment

Retail Pharmacy Chains

Under this scenario, the wholesaler sells the products to a retail pharmacy chain. The products are delivered to a central warehouse of the chain, and from there they are delivered to individual stores (see Figure 4).

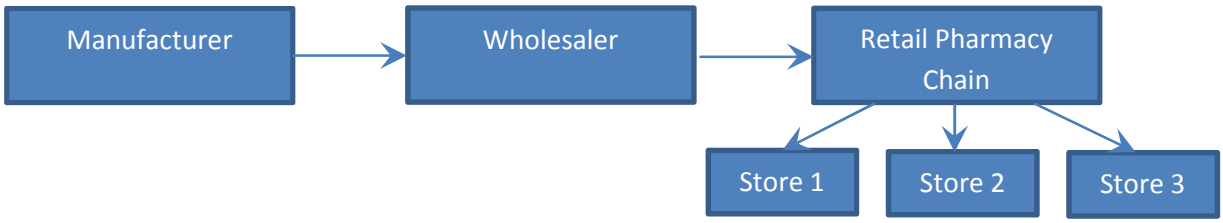

Figure 4: Supply Chain Involving Retail Pharmacy Chains

Repackaging

Under this scenario, the manufacturer packs the products in relatively large bottles (e.g. 100 count bottles), and ships them to a large wholesaler. The wholesaler will ship some of the products to a repackager, to repackage the products in smaller bottles (e.g. 50 count bottles). From there the products will be shipped to secondary wholesalers and independent pharmacies (see Figure 5).

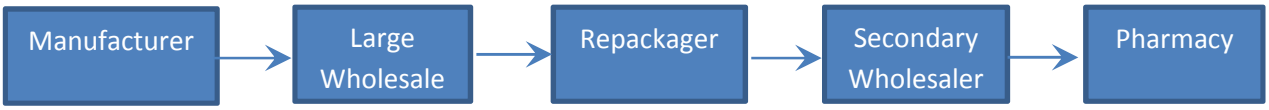

Figure 5: Supply Chain Involving Repackaging

Kitting

Under this scenario the manufacturer, or a third party, creates kits that combine multiple items packed together for a single use. For example, a kit may include a number of sterilized products to be used in an operation. The kits must remain closed and sealed until they reach their final destination and are opened for use. Each kit moves throughout the supply chain as a single unit. Since individual items within kits are excluded from pedigree requirements, a full kit will be the unit to be sampled and inspected as part of the proposed sampling model.

Inference in the U.S. Pharmaceutical Supply Chain[7]

In the pharmaceutical supply chain, individual bottles of medication usually move through the supply chain packed in an outer container, such as a pallet, case, or tote. The 2015 California state drug pedigree requirements mean that soon all individual items, to be sold in California, will need to be serialized and traced throughout the supply chain. Inference will help supply chain partners to leverage strong business practices and relationships to meet some of the challenges associated with these pedigree requirements.

[7] All information related to inference was taken from the document **"The Practice of Inference in the U.S. Pharmaceutical Supply Chain," published by GS1 US, May 2010.**

Inference refers to the practice of using other evidence, rather than opening the outer container and scanning each individual item, in order to verify the integrity of a shipment. Such evidence may include shipping documentation, physical inspection of the outer container, and existing trading partner relationships. Inference concludes when the outer container is opened and the serialized identifier for each item in the outer container is physically available to be read.

Inference is common in the pharmaceutical industry today in a non-serialized context, often for safety and security reasons, as open cases are vulnerable to tampering, theft and product mix-up. Moreover, many manufacturers today use tamper evident tape or seals to ensure the integrity of cases, and such cases remain sealed until items are staged for picking operations. Opening sealed cases negates the effectiveness of any such security feature. The practice of inference also helps products to move faster along the supply chain, and helps maintain cost-effective material handling.

Inference can be used under the following conditions:

- A collection (e.g. case, tote, or pallet) is present.
- The collection is identified with a unique serial number, and each item in the collection is also identified with a unique serial number.
- The hierarchical relationship of all serial numbers associated with the collection ("the aggregation") is recorded as the collection is built. This means that, while tagging items and packaging units, the supply chain partners should record all item-to-case/tote and case/tote-to-pallet hierarchies.
- The receiving supply chain partner receives an electronic communication detailing the aggregation of the collection.
- The receiving supply chain partner has assurance that the integrity of the collection has remained intact since leaving the last supply chain partner and can confirm that the integrity of the collection has not been compromised.

The use of inference remains an individual company decision. There are four factors that can be considered when deciding whether to use inference: trusted relationships, best practices, corroborative information, and physical security. Taking all these factors into consideration may significantly reduce the risk associated with inference.

Trusted Relationships: The relationship between supply chain partners can impact the decision about whether to use inference to a great degree. The level of trust in supply chain partner relationships can be established using a number of indicators including agreements; audit results; documented practices of the supply chain partner; and past performance as measured

by the historical accuracy of received documentation, shipment condition, and accuracy of received bundles.

Best Practices: Good business practices, at both a company and its supply chain partners, contribute to a secure supply chain practices. The level of trust in business practices can be established using a number of indicators such as supply chain partner score carding; performance auditing process; documented controls and standard operating procedures; routine capture of quality metrics to minimize "defects" of inbound and outbound product; implementation of process changes whenever process errors are detected in order to prevent future errors; and periodic review of processes for improvement opportunities.

Corroborative Information: Various types and sources of corroborative information can be used when determining whether inference would be appropriate. They may include: Physical inspection (original manufacturer tape intact, no signs of tampering, clean bill of freight, complete pedigree trail, confirmation of outer packaging identification against supporting documentation); delivery time consistent with expectations; electronic documents (e.g., EPCIS (Electronic Product Code Information Services) ship and receive information, pedigrees, advance ship notice, and bills of lading); and authentication capability.

Physical Security: Documented security policies and procedures within physical plants, distribution centers and facilities further contribute to establishing the trust to support the decision to use inference. Likewise, documented security policies and procedures for transport vehicles are an important consideration as well.

Statistical Acceptance Sampling – Overview

The term "Statistical" refers to the notion that the construction of acceptance sampling plans is based in large part on the law of large numbers and the mathematical theory of probability. This is in contrast to traditional sampling methods established without reference to the laws of probability, which are usually inferior to statistical sampling methods. For example, in the past, inspectors' decisions on the size and frequency of samples were likely to be influenced by their knowledge of the past quality history of the product being sampled. Such informal systems have obvious limitations, as they rely too much on individual inspectors and their memories of past quality history, and may lead to delays or failure to discover when quality has changed for the worse.

Although control charts and statistical types of acceptance sampling procedures were originally developed for use in mass production manufacturing, these techniques are applicable to most other types of activities in all sectors of the economy.

Statistical Sampling vs. 100% Screening

There are several advantages to inspecting only a sample of each incoming shipment rather than conducting 100% inspection of all incoming items. One obvious reason is that 100% inspection of all incoming shipments may be too costly and time consuming to be practical. Furthermore, the quality of the product accepted may actually be better with scientific acceptance sampling procedures, since, especially for large shipments, 100% inspection may lead to inspection fatigue, which may cause even the best inspectors to miss some of the nonconforming items. Another reason, which is relevant particularly in the pharmaceutical industry, is that opening pallets or cases for inspection requires the inspector to break any tamper-evident security features put in place by the manufacturer or the vendor. This in turn may make the items in those pallets/cases more vulnerable to theft and counterfeit. By sampling only a portion of the items, and keeping the rest of the pallets/cases intact, one can minimize these potential risks while still obtaining valuable information about the integrity of the products.

At the same time, while it is naturally desirable to accept only perfect shipments, one must recognize the fact that no sampling plan can ensure this. The statistical approach to acceptance sampling attempts to evaluate the risk assumed with alternative sampling procedures and to make a decision as to the degree of protection needed in any instance. It is then possible to choose a sampling acceptance scheme that gives a desired degree of protection with due consideration for the various costs involved. These costs may include the costs of the acceptance sampling program (inspection costs, and costs of administering the acceptance program); the costs resulting from accepting nonconforming items; as well as the potential economic implications of the inspection itself (e.g. risk of theft or tampering related to storing open cases of medication, costs related to a potential slower flow of material throughout the supply chain).

An important element of the selection of an acceptance inspection procedure should be the probable contribution of the procedure to reducing the percent of nonconforming items in the supply chain. The acceptance sampling system selected for this study, which is described in detail in the following section, has been successful in leading to such improvements.

Use of Acceptance Sampling Throughout the Supply Chain

Acceptance sampling not only reduces the risk of accepting shipments that contain nonconforming items, but it can also help in identifying the sources of these nonconformities. It is therefore highly recommended to conduct acceptance sampling inspections at each handoff in the supply chain—whenever products are delivered from one business partner to the next. Otherwise, if inspections take place infrequently, it may be very hard to trace back the source of nonconformities.

Statistical Sampling Model[8]

Background

The proposed statistical sampling system is based on the international standard ABC-STD-105, which was adopted by the U.S. military in 1963 and was designated as MIL-STD-105D[9]. It was adopted for commercial purposes in the U.S. by the American National Standards Institute in 1971 and designated ANSI/ASQC Z1.4. The standard is based on the concept of an Acceptable Quality Level (AQL), which will be discussed in more detail later in this chapter.

The ABC-STD-105 standard, as well as other statistical sampling systems based on the AQL, are widely known, and are used in purchases by governmental organizations, as well as for acceptance sampling of all kinds of products in the private industry.

Key Assumptions

There are a few important points to keep in mind while using the statistical sampling system:

1. It is assumed that when conducting incoming inspection, the integrity of the sampled items will be verified by examining their product pedigree. The product pedigree, which keeps a record of the product's entire path from its origin point at the manufacturer's site until its current location, is very valuable in verifying the integrity of the product. Still, it is important to note that such information will not be sufficient for identifying, for example, issues

[8] Most of the information related to the ABC-STD-105 standard – the standard that was the basis for the statistical sampling model proposed in this document – was taken from the book **Grant, Eugene L., and Leavenworth, Richard S., "Statistical Quality Control", 6th edition, McGraw-Hill Book Company, 1988**.

[9] This standard was first developed in 1960-1962 by the ABC Working Group, which included representatives from the military agencies of the U.S.A., Great Britain, and Canada. Its international designation was ABC-STD-105, until the International Standards Organization changed it to ISO 2859 in 1974.

related to mishandling of products during transportation (e.g., exposure of the medications to excessive heat).

2. As discussed earlier in this report, there are a number of factors that can be taken into consideration when deciding whether to use inference, including trusted relationships, best practices, corroborative information, and physical security. It is assumed, and strongly recommended, that companies use acceptance sampling *in combination* with these four factors rather than relying on just the acceptance sampling inspection for verifying the integrity of a shipment. That is, companies should first use these four factors to determine whether inference can be used reliably for a particular shipment. The company should inspect a sample of the incoming products as a second layer of assurance for the integrity of the shipment only after it is determined that it is sufficiently safe to use inference. If, on the other hand, there is a reason for the company to be suspicious about the integrity of an incoming shipment (e.g., if the outer packaging is damaged or the shipment arrives much later than expected), it is strongly recommended to conduct a full 100% inspection of the entire shipment.

3. Any sampling plan chosen will specify the sample size (number of items to be selected for inspection) and the acceptance number (the maximum number of nonconforming items allowed for a shipment to be accepted). When following a sampling plan, one should make a clear distinction between true counterfeits identified and nonconformities that are related to incomplete or inaccurate product pedigree. The rules in the selected sampling plan related to the acceptance number, and the switch between normal, tightened, and reduced inspection, are all based on the assumption that the nonconformities identified are related to the product pedigree. In the case of a true counterfeit being identified during incoming inspection, the receiving party should take *immediate steps* to address the issue based on the company's internal policy[10], rather than follow the instructions specified in the sampling plan. The issue of how to treat shipments that were found to contain a true counterfeit item is discussed in more detail later in the report.

Characteristics of the Proposed Statistical Sampling System

Acceptable Quality Level

The Acceptable Quality Level (AQL) is the percent nonconforming that, *for acceptance sampling purposes only*, is considered acceptable as a process average.

[10] The process of how to treat a true counterfeit may vary from company to company, and the actions taken may also vary based on inputs received from the FDA or DEA in each instance.

The first decision to be made when implementing the statistical sampling system concerns the acceptable quality level. The AQL may be identical for all vendors and products or, if preferred, may have different values for different product families or different vendors. In this study, it was assumed that all pharmaceutical products will have the same AQL.

Normal and Tightened Inspection

The proposed statistical sampling system uses two types of inspections, namely *normal* and *tightened*. Normal inspection is selected in the absence of unsatisfactory quality history or other reasons for misgivings about the quality of the submitted product, and is designed to protect vendors with satisfactory quality history against the rejection of shipments that have a percent nonconformities equal to or better than the stated AQL.

However, such acceptance criteria generally give the receiving party insufficient protection against accepting shipments that are moderately, or sometimes considerably worse than the AQL. For this reason, tightened inspection, which is based on more severe acceptance criteria designed to protect the receiving party, must be used whenever the quality history is unsatisfactory, unknown, or when there are other reasons for being suspicious about quality.

In addition to normal and tightened inspection, the sampling plan may also use *reduced inspection*, if desired (the concept of reduced inspection will be discussed later).

Criteria for shifting to tightened inspection and requalification for normal inspection: Based on the ABC-STD-105 standard, one should shift from normal to tightened inspection when two or more out of the last five consecutive shipments from the same supplier have been rejected on original inspection[11].

When tightened inspection is in effect, normal inspection shall be reinstituted when five consecutive shipments from the same supplier have been considered acceptable on original inspection. If, however, a rejection of one or more shipments under tightened inspection have prevented a shift back to normal inspection, then after tightened inspection has been in effect for 10 consecutive shipments from the same vendor, sampling inspection should be terminated until action is taken to improve the quality of incoming shipments from that vendor.

Probabilities of switching between normal and tightened inspection: The probability of switching from normal to tightened inspection is the probability that two or more of five

[11] The term **original inspection** refers to the first time an incoming shipment is inspected. Shipments that were initially rejected, but were later accepted after additional information was provided by the vendor or after any other issues with the identified nonconforming items were resolved, should be counted as “rejected” in this context.

consecutive shipments will be rejected on normal inspection. This can be calculated as 1 minus the probability that zero or one shipments will be rejected:

$$P(\text{N} \rightarrow \text{T}) = 1 - (P_{a,N})^5 - 5\,(P_{r,N})\,(P_{a,N})^4$$

Where: $P_{a,N}$ = probability of acceptance on normal inspection
$P_{r,N}$ = probability of rejection on normal inspection

The probability of switching from tightened to normal inspection after the first five shipments have been inspected on tightened inspection is equal to the probability that all five shipments will be accepted:

$$P(\text{T} \rightarrow \text{N}) = (P_{a,T})^5$$

Where: $P_{a,T}$ = probability of acceptance on tightened inspection

For example, for shipment sizes between 3,201-10,000 and an AQL of 1.0%, the following probabilities apply[12]:

Incoming quality:	**½ AQL = 0.5%**	**AQL = 1.0%**	**2 AQL = 2.0%**
$P_{a,N}$	0.999	0.983	0.785
$P_{a,T}$	0.981	0.857	0.433
$P(\text{N} \rightarrow \text{T})$	≈ 0	0.0028	0.2937
$P(\text{T} \rightarrow \text{N})$	0.9085	0.4623	0.0152

Table 1: Switching Probabilities at Various Quality Levels; AQL = 1%, Shipment Size Between 3,201-10,000

These probabilities demonstrate that, when the quality level is at the AQL or better, a switch from normal to tightened inspection is quite unlikely. However, once the switch is made, there is a chance of less than 50% that a return to normal inspection will be made unless product quality improves to a level better than the AQL.

Reduced Inspection

Unlike normal and tightened inspection, the use of reduced inspection is optional. The acceptance criteria under reduced inspection are less stringent compared to normal inspection, and will often allow a smaller sample size compared to normal inspection. A switch to reduced inspection will therefore help the receiving party reduce their inspection cost, and focus their attention and resources on those shipments that are coming from unknown or less reliable suppliers.

At the same time, under reduced inspection, shipments that contain nonconforming items have a greater chance of not being rejected, compared to normal inspection. It is therefore

[12] For details of the sampling plans under this scenario, please refer to the Excel model.

recommended for companies to be cautious when considering the use of reduced inspection, and to allow this type of inspection only when they feel confident that the high quality of incoming shipments observed so far is likely to continue (for example, when the source of supply as well as the entity in charge of transportation are known to be very reliable and when total transportation time is very short). In all other cases, it may be best to avoid using reduced inspection, and limit the sampling plan to normal and tightened inspection only.

Criteria for shifting to reduced inspection, and back to normal inspection: In general, eligibility for reduced inspection should be based on recent quality history indicating average quality considerably better than the AQL. Moreover, it should seem likely that the product to be inspected under reduced inspection will be produced and delivered to the receiving party under the same conditions that gave rise to the recent good quality history.

More specifically, based on the ABC-STD-105 standard *all* the following conditions must be met for a shift from normal to reduced inspection:

1. The preceding 10 shipments (or more, as indicated in the Excel model, Table 5[13]) have been on normal inspection and none has been rejected on original inspection; and
2. The total number of nonconforming items in the samples from the preceding 10 shipments (or such other number of shipments as was used for condition (1) above) is equal to or less than the applicable number given in Table 5; and
3. It seems likely that the product to be inspected under reduced inspection will be produced and delivered to the receiving party under the same conditions that gave rise to the recent good quality history; and
4. Reduced inspection is considered desirable by the responsible authority.

Normal inspection must be reinstated whenever *one* of the following conditions is met:

1. A shipment is rejected; or
2. A shipment is accepted but the number of nonconforming items found is between the acceptance number *(Ac)* and the rejection number *(Re)*[14]; or
3. Issues arise in the production and distribution process that may raise concerns regarding the integrity of incoming shipments; or
4. Other conditions warrant that normal inspection shall be instituted.

[13] Table 5, "Limit Numbers for Reduced Inspection – ABC-STD-105" can be found in the Excel model, under the "Supporting Tables" tab. The instructions provided under the "Sampling Model" tab are based on this table.
[14] The acceptance and rejection numbers are specified in the Excel model, based on the parameters of the selected sampling plan. They can be found under "Reduced Inspection" in the "Sampling Model" tab.

Selecting an AQL: Quality and Other Characteristics of the Sampling Plan

As mentioned earlier, the first decision to make, before using the sampling model on a regular basis, is the appropriate Acceptable Quality Level to use. When analyzing and evaluating sampling plans associated with different values of AQL, it is of value to take into consideration a number of factors related to quality and cost, which are a function of the selected AQL. The following is a description of several such factors, which are also calculated and displayed in the Excel model.

Operating Characteristic (OC) Curve

An OC curve shows graphically the relationship between the percentage of nonconforming items in the submitted shipments and the proportion of inspected shipments that will be accepted *in the long run* (usually referred to as the *probability of acceptance*). In other words, if an incoming shipment is expected to have a specific percent nonconforming, one can determine from the OC curve what the probability of accepting that shipment would be, based on the proposed sampling plan.

The OC curve demonstrates the ability of the sampling plan to distinguish between good shipments (with an acceptable level of nonconforming items) and bad shipments. In principal, the steeper the OC curve, the better the ability of the sampling plan to distinguish between good and bad shipments.

The Excel diagram related to the OC curve includes four different curves: one for normal inspection, one for tightened inspection, and two for reduced inspection. When evaluating the sampling plan associated with a specific AQL, one should take into consideration all four curves (or only those related to normal and tightened inspection, if a decision has been made not to use reduced inspection).

Average Outgoing Quality (AOQ)

The AOQ calculates the long-term expected percent nonconforming in shipments *after inspection*. It is based on the assumption that each shipment that passes the original inspection will contain approximately the percent nonconforming submitted (actually slightly less, given that any nonconforming items found during the inspection will be removed or fixed). At the same time, it is assumed that each shipment that does not pass the original inspection will go through 100% screening, and that all nonconforming items found will be fixed or replaced with good items. Therefore, in the long run, the average outgoing quality (AOQ) after inspection will be equal to:

$$AOQ = (P_a) * (100p) + (1 - P_a) * 0 = (P_a) * (100p)$$

Where P_a is the probability of acceptance of a shipment and *100p* is the percent nonconforming in an incoming shipment.

These calculations are based on a few simplifying assumptions:

1. All incoming shipments have the same size *N*.
2. The 100% screening inspection finds all nonconforming items, and these items are either replaced with good ones or are fixed (if the nonconformity was related to the data in the product pedigree).

It should be emphasized that any calculations of average outgoing quality give the expected quality in the long run. For a single shipment or over a short period of time the outgoing quality may be better or worse than the long-run average.

Average Outgoing Quality Limit (AOQL)

The average outgoing quality limit (AOQL) is the maximum value of AOQ across all values of *100p*. That is, in the long run, and regardless of the incoming quality submitted, the outgoing quality after inspection will not be worse than the sampling plan's AOQL. In fact, in most cases the AOQ will be much lower than the AOQL.

The AOQL for normal, tightened, and reduced inspection are all calculated In the Excel model. Since the sampling plan will always use both normal and tightened inspection, and potentially also reduced inspection, the value of the AOQL for the entire plan will lie somewhere between the individual AOQL values for the different types of inspection.

Consumer's Risk and Producer's Risk

There are always two parties to an acceptance procedure, the party that ships the products, and the party that receives the shipment. For convenience, the discussion in this section refers to the shipping party as the "producer," and to the receiving party as the "consumer."

The consumer requires protection against acceptance of too many nonconforming items. At the same time the producer needs to be protected against the rejection of too many shipments with a sufficiently good quality level. When selecting a sampling plan, one should balance between these two objectives.

Consumer's risk: In order to calculate the consumer's risk, one should first specify the quality level that is considered undesirable[15]. The consumer's risk, α, will then be equal to the

[15] It is customary to specify an undesirable quality level that is significantly lower than the stated AQL (for example, at least 4 to 5 times the value of AQL, for the relatively low AQL values). Otherwise, it will be impossible to achieve a reasonable level of consumer's risk through sampling, and consequently all incoming shipments will likely have to go through 100% screening.

probability of accepting a shipment that contains the specified undesirable percent nonconforming.

Producer's risk: In general, the producer's risk, β, equals to the probability of rejecting a shipment that is actually at a sufficiently good quality level. In the Excel model, that desirable quality level is set to equal the selected AQL. That is:

$$\text{Producer's Risk} = \beta = 1 - P_a(AQL)$$

Where $P_a(AQL)$ is the probability of accepting a shipment with a percent nonconforming equal to the AQL.

Impact of sample size on consumer and producer's risk: The sample size will have a direct impact on the level of risk borne by the consumer and producer. In general, larger sample sizes (which are associated with larger shipments) will provide better protection to both trading partners, as they will result in fewer good shipments being rejected and fewer bad shipments being accepted.

To illustrate this point, consider the example where the AQL is set to equal 1%. Under the proposed sampling system, the producer's risk at the AQL value in normal inspection varies from 12.3% for plans with the smaller samples sizes where $c = 0$, to 0.9% for the large sample sizes and acceptance numbers. As for the consumer, if we set the undesirable quality level to equal 3.5%, then the consumer's risk of accepting shipments with 3.5% nonconforming under normal inspection will range from approximately 63% for very small samples, to 0.01% for very large samples. Figure 6 illustrates this point.

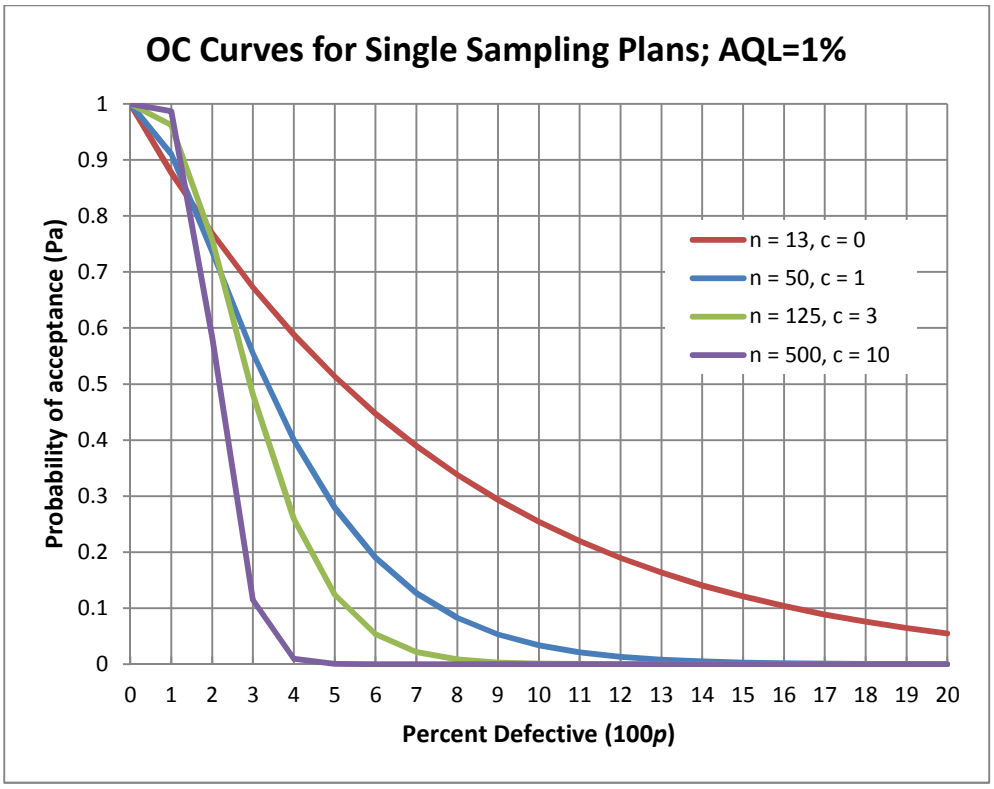

Figure 6: OC Curves for Four Different Single Sampling Plans, All With an AQL of 1%

Average Total Inspection (ATI) and Average Fraction Inspected (AFI)

These two parameters calculate the average total number of items inspected per shipment, and the ratio between this number and the size of the entire shipment. When evaluating different sampling plans, one should take into consideration the value of these parameters in addition to the outgoing quality associated with each plan, since they are likely to have a direct impact on the inspection cost associated with the sampling plan.

Under the assumption that each rejected shipment will go through 100% inspection, then the average total number of items to be inspected (ATI) per shipment will be equal to:

$$ATI = n * (P_a) + N * (1 - P_a) = n + (N - n) * (1 - P_a)$$

Where:

P_a = the probability of acceptance of a shipment;

N = the total number of items in the incoming shipment;

n = the number of items in the sample.

The average fraction inspected (AFI) will then be equal to:

$$AFI = ATI / N.$$

Using the Statistical Sampling Model on a Regular Basis

Diagram 1 summarizes how the sampling model should be used on a regular basis. It is followed by a more detailed discussion of some aspects of the process.

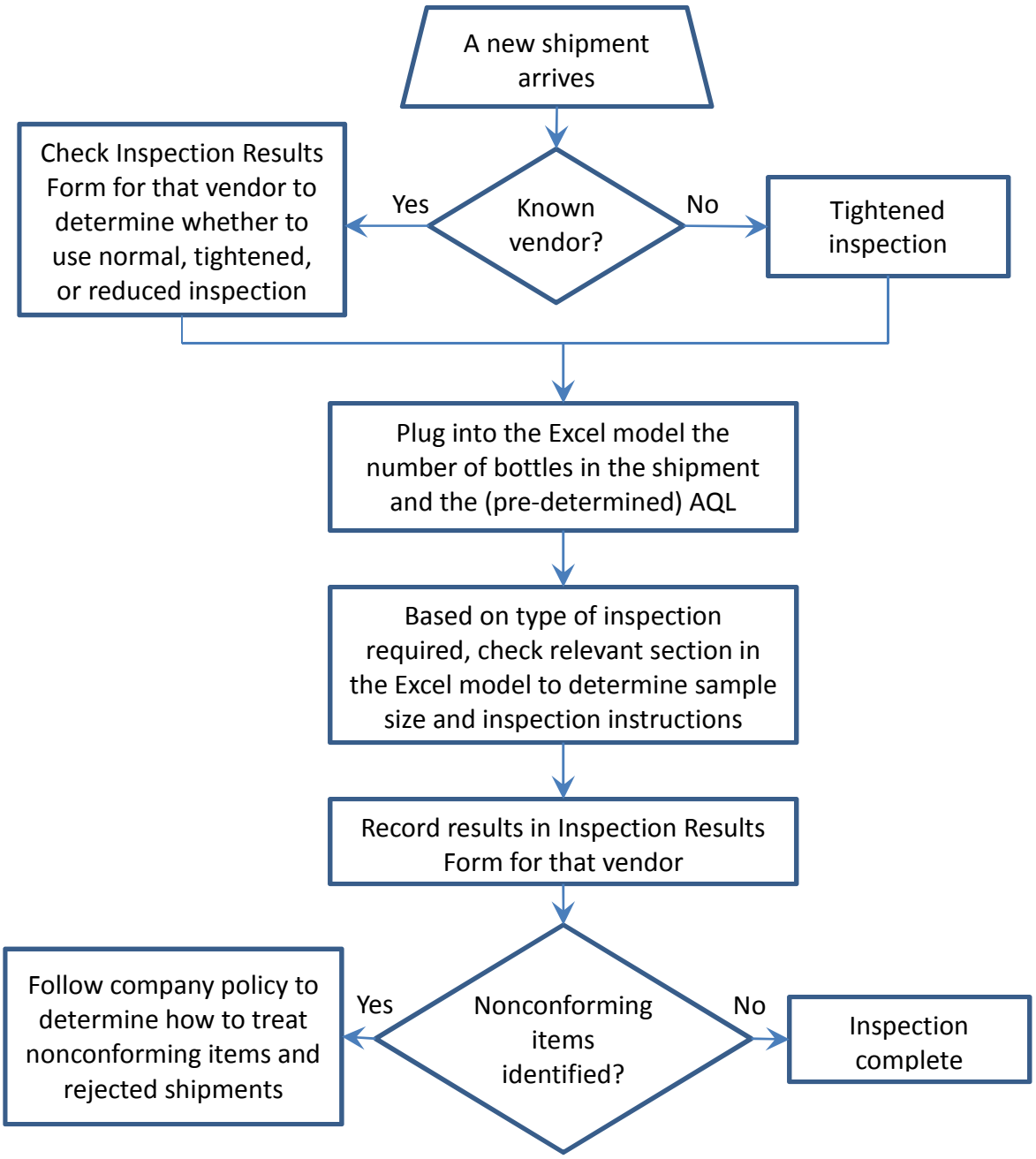

Diagram 1: Process Flow for Using the Statistical Sampling Model

Grouping Shipments for Inspection

An *inspection lot* is defined as a group of items accepted or rejected on the basis of a single sample. To get the best results from acceptance sampling, two rules should govern decisions on this matter, namely:

1. Within each inspection lot, the factors that seem likely to cause marked variability in quality should be as nearly constant as practicable.
2. Subject to the limitations of rule (1), inspection lots should be as large as possible.

Different shipments from the same vendor may vary in such factors as the origin point of the shipment (if, for example, the vendor has multiple warehouses or distribution centers), the origination sources of the products (for example, if the vendor is a wholesaler with multiple sources of supply), the party responsible for transportation, and the shipping route. To minimize the variability within each inspection lot, it is therefore recommended that the receiving party inspect each incoming shipment separately.

When the size of incoming shipments is very small, it may make any form of sampling inspection impractical. In such cases it may be best for the receiving party to resort to 100% inspection.

Shipment Size to Be Measured in Bottles/Cartons

While large wholesalers may receive from the manufacturer medications packed in full pallets, as the items move throughout the supply chain, the pallets will very quickly be broken down to cases and single items (bottles or cartons). To keep things consistent, the Excel model uses single items as the unit of measurement. That is, the model requires as an input the shipment size in bottles/cartons, and will then determine the sample size in bottles/cartons as well.

Shipments Received From a New or Unknown Vendor

Given the potential severe consequences of nonconforming pharmaceutical products reaching the end consumer, it is recommended, at the very minimum, that companies in the pharmaceutical industry use tightened inspection whenever dealing with an unknown vendor. If the receiving party has very little or no information about the vendor and his practices, it may even be better to conduct 100% inspection of at least the first shipment received from that vendor. This is in contrast to the recommendation in the ABC-STD-105 standard, according to which normal inspection should be used for the first shipments received from new or unknown vendors (which essentially gives the vendor the benefit of the doubt).

If the quality of the products shipped by the new vendor is consistently satisfactory, then after five accepted shipments the vendor will be qualified for normal inspection.

Infrequent/Isolated Shipments

The proposed sampling system is constructed in such a way that ensures that *in the long run* the average outgoing quality will be close in value to the chosen AQL. However, when shipments are isolated or infrequent, a sampling plan based on a desired AQL value will not give the receiving party a sufficient level of protection. The reason for that is that under normal inspection, the parameters of the sampling plan are chosen so that nearly all shipments at a quality level equal to or better than the AQL will be accepted, which means that shipments with a quality level slightly worse than the AQL will also have a relatively high probability of being accepted.

When determining the course of action for isolated shipments, one should distinguish between trusted and unknown vendors. Whenever an isolated shipment is received from an unknown vendor, the receiving party should be willing to conduct a 100% screening of the shipment. If, on the other hand, an isolated shipment is received from a trustworthy vendor, 100% inspection of the entire shipment may not be necessary. Instead, the receiving party may select a sampling plan based on the overall level of protection it provides as indicated by its OC curve, with a particular focus on its associated consumer's risk.

For example, suppose that a shipment of 1,000 bottles is received. The receiving party considers 5% nonconforming to be unacceptable, and requires the probability of accepting a shipment with such a percent nonconforming to not exceed 1.5%. It turns out that for a shipment of this size, normal inspection associated with an AQL=0.4% will result in a 1.24% probability of accepting a shipment with 5% nonconforming. This probability is smaller than the required consumer's risk of 1.5%, and therefore it should be sufficiently safe for the receiving party to use a sampling plan based on this AQL. The sampling plan in this case will be to sample and inspect 125 items, and accept the shipment if no more than one nonconforming item has been identified[16].

Mixed Shipments

It is assumed that all pharmaceutical products in the scope of this study should have the same AQL. That is, nonconformity is considered as having the same level of severity regardless of the type of product under consideration. Under this assumption, all incoming shipments should be treated the same when determining the required sampling plan. This means that regardless of the number of types of products in an incoming shipment, the sampling plan (sample size and acceptance number) should be determined based on the total number of bottles in the shipment. In addition, the items for inspection should be sampled randomly from the entire shipment, without consideration to the types of products in the sampled bottles. Changing this

[16] For details of the sampling plan under this scenario, please refer to the Excel model.

assumption will require grouping the incoming products based on their related AQL, and inspecting each group separately.

Sampling Items for Inspection – the Importance of Randomness

The calculations used to compute the probability of acceptance of an incoming shipment with a given quality, and the construction of the related OC curves, are based on the assumption that samples are drawn at random. That is, it is assumed that each item in the shipment has an equal chance to be selected in the sample. If the items in a shipment have been thoroughly mixed, a sample chosen anywhere in the shipment meets the requirement of randomness. However, most likely it will not be practical to thoroughly mix all items in a shipment before a sample is drawn. Still, at minimum one should avoid any obvious type of bias when drawing a sample. For example, if items are packed in layers, then an effort should be made to select items for inspection from all layers and from different locations within each layer. Similarly, if items are packed in cases, then the sample should be drawn from multiple cases.

In large shipments, the difficulties of random selection may be so great that it is advisable to adopt stratified (proportional) sampling. To do that, one should:

1. Divide the entire shipment into sub-groups on the basis of factors that are likely to lead to variation in the quality of the product.
2. From each sub-group select a sub-sample, with a size that is proportional to the size of the sub-group in the entire shipment.
3. As much as possible, draw the sample items from each sub-group at random.

Treating Nonconforming Items and Rejected Shipments

Generally speaking, an item can fail incoming inspection because of two main reasons: the item is a true counterfeit, or the pedigree associated with the item is incomplete or inaccurate[17].

In the case of a true counterfeit, the receiving party should immediately engage the processes called for based on the company's internal policy. These policies may vary from company to company, and may include such steps as notifying the FDA or DEA, placing all counterfeit items in quarantine, and putting on hold all future shipments from that vendor until the authorities are alerted.

If, however, the issue is with the product pedigree rather than with the product itself, then it is recommended that the receiving party contact the vendor and request the missing pieces of information, so that the product pedigree can be completed. If an entire shipment has been

[17] As a reminder, it is assumed that companies will use statistical sampling only after determining that it is sufficiently safe to use inference, based on such factors as trusted relationships, best practices, corroborative information, and physical security.

rejected after too many items with incomplete pedigree have been identified during inspection, the receiving party can respond it two ways: (1) internally conduct 100% screening of all items in the rejected shipment, and contact the vendor for more information for all nonconforming items that have been identified; and (2) send back the entire shipment to the vendor, and require the vendor to conduct the 100% screening and update the pedigree records.

During the early phases of the serialization/track and trace/pedigree program, and later on when instances of data inaccuracies are infrequent, it may be best for the receiving party to follow option (1), and conduct the 100% screening internally. This way, delays and transportation costs can be minimized. If, however, shipments from some vendors continue to frequently be rejected due to data inaccuracies, it may be better for the receiving party to send back all rejected shipments to the vendor, as the rejection of entire shipments will bring much stronger pressure on the vendor to improve the integrity and completeness of the data.

Systematic Recording of Inspection Results

The AQL acceptance sampling plan requires recording of the results of all incoming inspections, in order to determine whether to use normal, tightened, or reduced inspection. The Excel model includes a suggested form to be used for this purpose (see Inspection Results Form tab). Such a form should be completed separately for each of the vendors the company works with. For each shipment, the inspector should record the details of the shipment (date, shipment size, products inspected), the sampling plan used (type of inspection, AQL, sample size, etc.), and the result of the inspection (number of nonconforming items found, shipment accepted/rejected). In addition, based on the history of the last few shipments, it should be determined what type of inspection should be used for the next shipment from that vendor.

An added benefit of such records is that they may help to bring out the differences between the performance levels of different vendors. In addition, and especially in the early stages of the implementation of the serialization/track and trace/pedigree program, the records of inspection results may help identify those companies that seem to be struggling more with ensuring the integrity or completeness of the pedigree of the products they sell. Attention can then be focused on helping out those companies.

As for true counterfeits, sampling inspection may help identify not only bad vendors, but also transportation companies or shipping routes that may be more vulnerable.

Excel Model

As part of this study, an Excel model was developed to help users determine the best AQL to use, and the specific sampling plan for each incoming shipment. The Excel model includes the following parts (tabs):

Instructions: Includes information for users on how to use the Excel model.

Sampling Model: This is the main part of the Excel model. Users should use this part to input the shipment size of each incoming shipment and the AQL, and determine the details of the related sampling plan (sampling size and acceptance number). In addition, in this part, users can view quality and other characteristics associated with the selected sampling plan.

Diagrams: Includes a schematic diagram of the rules for switching between normal, tightened, and reduced inspection.

Inspection Results Form: Includes a proposed form to be used for recording the inspection results of incoming shipments. A separate form should be used for each vendor.

Model Assumptions: Provides information on some of the underlying assumptions related to the calculations associated with the sampling model.

Supporting Tables: Includes the master tables, taken from the ABC-STD-105 standard. These tables specify all the sample plans associated with each AQL and shipment size.

Construction of the Statistical Sampling Model

A number of decisions had to be made while structuring the proposed statistical sampling model. The following is a short explanation of the logic behind these decisions.

Choosing Among Single, Double, and Multiple Sampling

When selecting a sampling system, one of the decisions to make is whether to use a single, double, or multiple sampling plan. This decision will dictate the maximum number of samples to be inspected before deciding whether to accept a shipment or reject it:

- **Single sampling plan**: the decision is always based on the evidence of only one sample.
- **Double sampling plan**: involves the possibility of delaying the decision on the shipment until a second sample has been taken.
- **Multiple sampling plan**: when three or more samples of a stated size are permitted before a decision is made.

In all AQL systems, an attempt has been made to match OC curves as closely as practicable among the single, double, and multiple sampling plans for any stated shipment size and AQL. This means that the choice among single, double, and multiple sampling plans should not be based on the expected outgoing quality, which is similar under all plans, but rather on other considerations.

The main advantage of using double or multiple sampling plans is a reduction in the expected average total number of items to be inspected. On the other hand, the administration of plans becomes more complicated as the number of stages allowed in the sampling plan increases, and it may be more difficult to train inspectors to use double/multiple sampling correctly. In addition, double and multiple sampling plans are likely to increase the variability of inspection load, which may make it more difficult to schedule inspectors' time. For these and other reasons, it was decided to base the sampling system recommended in this study on a single sampling plan.

Choosing Inspection Level

The ABC-STD-105 standard offers three general inspection levels (I, II, and III), and four special inspection levels (S-1 through S-4) to choose from. The discriminatory power of the sampling plans increases from level I to III (that is, the OC curve becomes steeper). The default among these three inspection levels, which is most commonly used, is level II. The special inspection levels S-1 to S-4 have less discriminatory power, and are employed when small sample sizes are necessary and when large sampling risks can or must be tolerated. This will be the case, for example, with destructive inspection[18,19]. Since the type of inspection to be conducted for the pharmaceutical products is not destructive, there is no reason to use the special inspection levels. It was therefore decided to base the sampling system recommended in this study on general inspection level II, which, as mentioned earlier, is the most commonly used.

The Use of Binomial Distribution to Calculate Probabilities of Acceptance

The most accurate way to calculate the probability of selecting a sample with a specific number of nonconforming items out of an entire shipment with a known percent nonconforming is by using the hypergeometric probability function. However, the extensive use of factorials in the calculations makes the hypergeometric probability function impractical to use in most situations. The binomial distribution, which is based on the assumption that the probability of a nonconforming item is constant from draw to draw, often provides a good enough approximation to serve as a practical basis for evaluating incoming shipments. To keep the Excel model flexible, all calculations related to the probability of selecting a sample with a specific number of nonconforming items were based on the binomial distribution. The larger a

[18] In destructive inspection, the items inspected are damaged during inspection is such a way that prevents them from being used afterwards.

[19] Source: Mittag, H.J., and Rinne, H., "Statistical Methods of Quality Assurance," Chapman & Hall, 1st English language edition, 1993.

shipment compared to its sample size, the closer the binomial approximation will be to the true probability value[20].

A Few Comments Regarding Statistical Sampling

Characteristics of Sample Size

In the past, a common practice has been to specify that the sample inspected should be some fixed percentage of an incoming shipment, such as 5, 10, or 20 percent. This specification was generally based on the mistaken idea that the protection given by sampling schemes is constant if the ratio of sample size to shipment size is constant. But this assumption is wrong, as is illustrated in Figure 7.

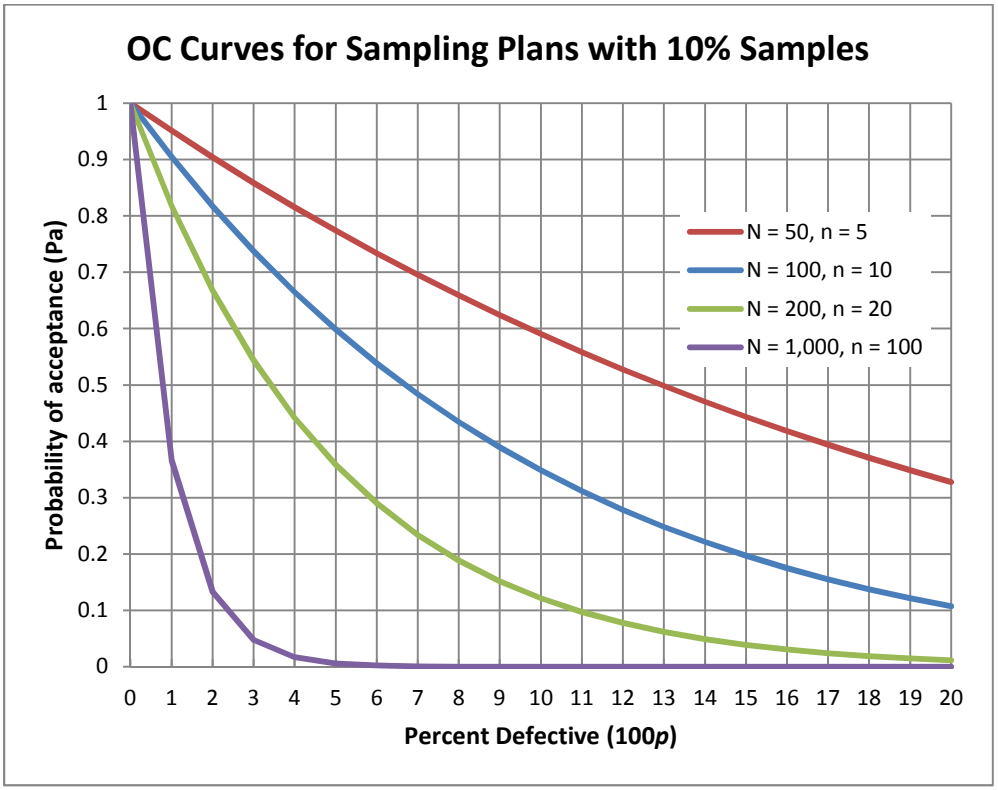

Figure 7: OC Curves for Four Single Sampling Plans, All With 10% Sample and Acceptance Number *c = 0*

The figure compares the OC curves of four sampling acceptance plans, all of which involve a 10% sample and an acceptance number of zero. It is clear that the plans with a higher sample size provide a much better quality protection. In fact, the absolute size of a random sample is much more important than its relative size compared to the size of the entire shipment in determining the extent of quality protection provided by an acceptance sampling plan.

[20] More information on these two probability functions can be found in the Excel model, under the Model Assumptions tab.

Acceptance Number

At times, people may be reluctant to select a sampling plan with an acceptance number larger than zero (that is, a plan that allows the acceptance of shipments for which one or more nonconforming items were identified during incoming inspection). With this regard, one should keep in mind two things. First, as is illustrated in Figure 7, even a perfect sample, with zero nonconforming items, does not ensure a perfect shipment. Therefore sampling plans with acceptance numbers larger than zero should not be treated differently than plans that permit only shipments with a perfect sample to be accepted. Moreover, for a desired level of protection against accepting shipments with a low quality level, larger acceptance numbers will involve larger sample sizes. And since plans with larger sample sizes will have steeper OC curves, these plans will actually have greater ability to discriminate between satisfactory and unsatisfactory shipments.

Numerical Example

The following example illustrates the use and the value provided by the statistical sampling model. The details of the example can be checked with the help of the Excel model.

Details of the Incoming Shipment

Suppose that a wholesaler receives an incoming shipment that contains 3,000 bottles of medication. The wholesaler has specified his acceptable quality level to be equal 0.4%, which means that *for acceptance sampling purposes only*, the wholesaler considers an average of 0.4% nonconforming items in incoming shipments to be acceptable.

The shipment has arrived from a vendor with whom the wholesaler has long standing good relationship.

Sampling Plan

Based on the inspection results of past shipments received from the same vendor, the inspection plan for the current shipment should be based on Normal inspection. For a shipment size of 3,000 bottles and an AQL of 0.4%, the parameters of the sample plan are:

Sample size: $n = 125$ bottles
Acceptance number: $c = 1$

That is, 125 bottles, which represent 4.2% of the entire shipment, should be selected randomly from the shipment and be inspected. The shipment will pass inspection only if at most one of the 125 inspected items was found to be nonconforming. If more than one nonconforming item has been identified, the entire shipment should be rejected.

Plan's Ability to Identify "Bad" Shipments

Figure 8 shows the OC curves associated with all the inspection plans related to a shipment size of 3,000 bottles and AQL of 0.4%. The red curve represents the OC curve for Normal inspection.

Consumer's Risk: Suppose that the wholesaler considers a level of 3.5% nonconforming items in an incoming shipment to be totally unacceptable. The probability of accepting an incoming shipment with this percent nonconforming under normal inspection is only 6.4%. This probability goes down to 0.7% under tightened inspection. If a level of 2% nonconforming items is considered unacceptable, the probabilities of acceptance will be equal to 28.4% and 8.9% under normal and tightened inspection respectively.

Producer's Risk: As for the vendor, the probability that a shipment that contains no more than the AQL level of 0.4% nonconforming will be rejected is equal to 9% under normal inspection, and to 19.1% under tightened inspection.

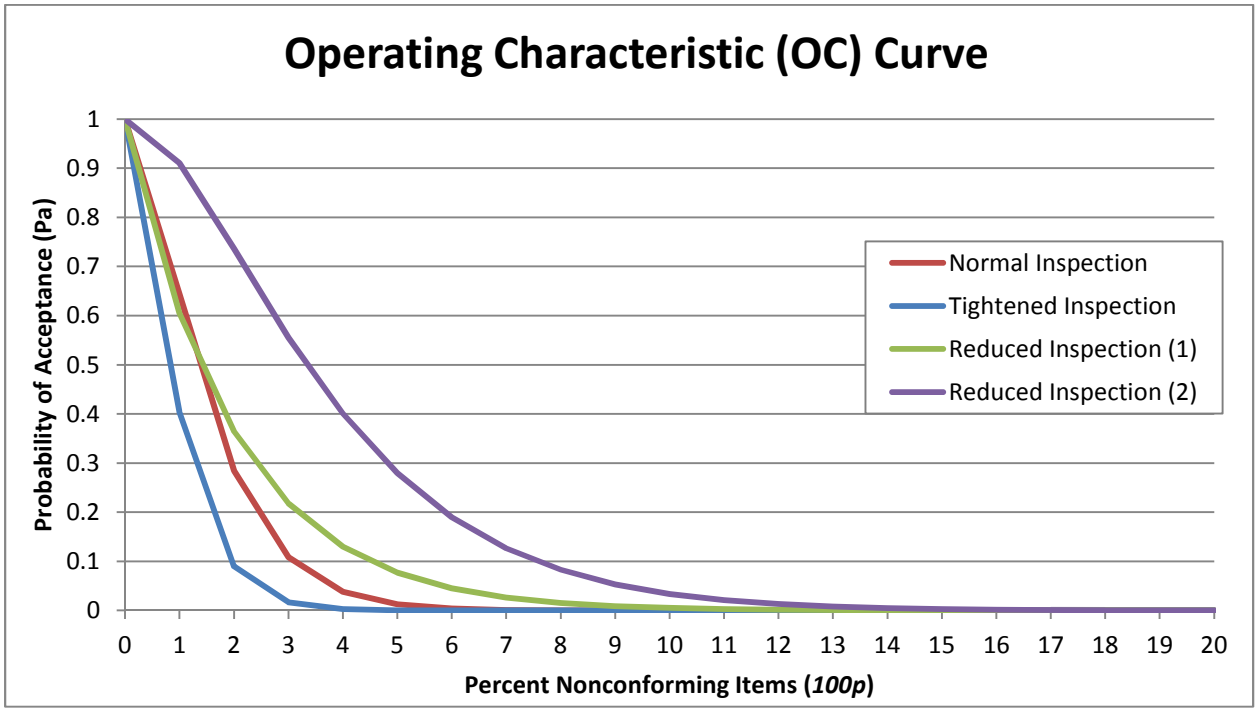

Figure 8: OC curves for shipment size *N = 3,000* and *AQL = 0.4%*

Average Outgoing Quality

Figure 9 shows the average outgoing quality under normal, tightened, and reduced inspection, in the long run, as a function of the actual quality of incoming shipments.

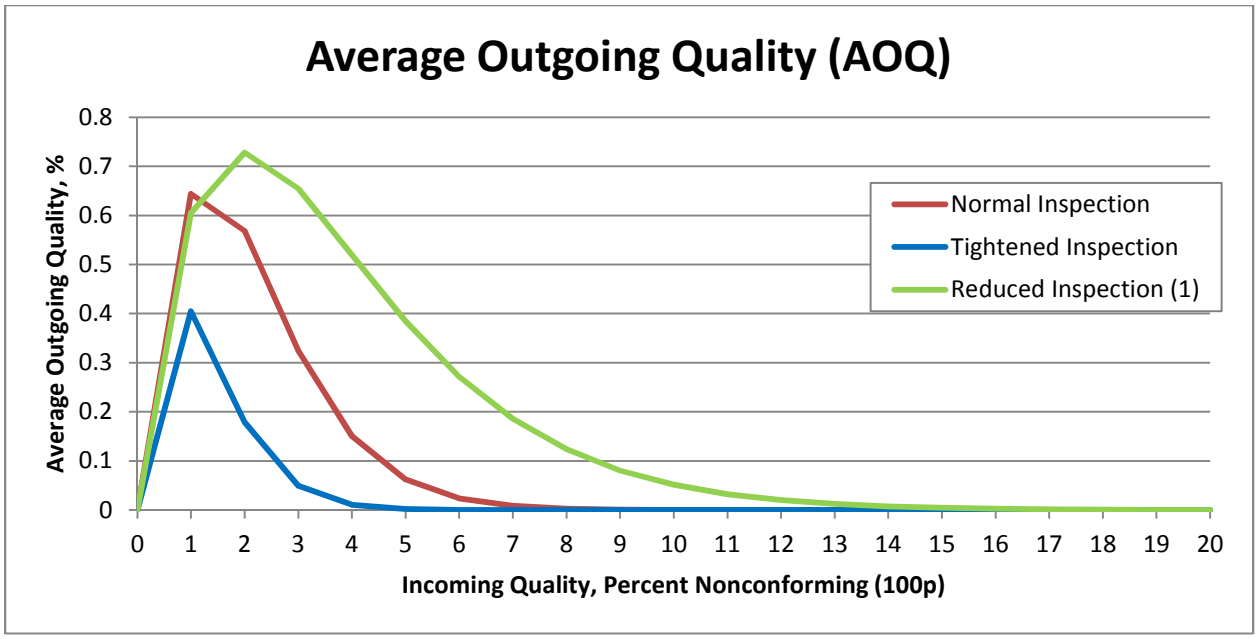

Figure 9: Average Outgoing Quality Curves for Shipment Size *N = 3,000* and *AQL = 0.4%*

As can be seen from the diagram, the average outgoing quality limit under normal inspection is 0.64%, and this number goes down to 0.4% under tightened inspection. This means that, assuming that all incoming shipments are of size *N=3,000*, then under normal inspection, and regardless of the quality of incoming shipments, in the long run the average percent of nonconforming items will not exceed 0.64% after inspection.

Inspection Rate

As mentioned earlier, the sample size of 125 items represents 4.2% of the entire shipment size. In the long run, and assuming that the wholesaler will conduct 100% inspection of all items in shipments that do not pass the initial incoming inspection, then the average total number of items inspected per shipment will be equal to 383 bottles under normal inspection, or 12.8% of the entire shipment.

Summary

This example demonstrates the power of statistical acceptance sampling. By using a sampling plan that calls for the initial inspection of 125 bottles, or 4.2% of the entire shipment of 3,000 bottles, the wholesaler was able to verify that in the long run, and regardless of the actual quality of incoming products, the average percent nonconforming items *after inspection* will not exceed 0.64%.

Summary and Future Recommendations

While overall the pharmaceutical supply chain in the United States is very secure, it is not completely immune to drug counterfeiting. In particular, the practice of inference – which carries with it many benefits as it reduces the chance for tampering, theft, and product mix-up by keeping cases sealed as long as possible – may still provide a small chance for counterfeit products to be introduced into the supply chain.

To address this concern, and allow companies to continue using inference while limiting the risks associated with this practice, a statistical sampling model was developed in this study, based on the international standard ABC-STD-105 (also known as MIL-STD-105D, ANSI/ASQC Z1.4, and ISO 2859). The characteristics of the model and detailed information on how to use it are included in this report. The report also provides a brief explanation of some of the decisions that were taken while constructing the sampling model. A related Excel model allows users to determine the specific sampling plan for each incoming shipment and includes some key statistics related to the selected plan.

While using the statistical sampling model, it is important to keep in mind that the model only ensures that *in the long run* the average outgoing quality will be close in value to the chosen AQL. For isolated or infrequent shipments, a sampling plan based on a desired AQL value may not give the receiving party a sufficient level of protection. In those cases, the receiving party should either conduct 100% screening of the entire shipment or select a sampling plan based on the overall level of protection it provides as indicated by its OC curve.

It is highly recommended that pharmaceutical companies use the statistical sampling model throughout the supply chain, whenever products are delivered from one business partner to the next. In addition, it is recommended to use the sampling model only after verifying, based on various factors such as the ones mentioned in this report, that it is sufficiently safe to use inference. That way, companies should be able to increase confidence in the security of the supply chain, while still maintaining most of the benefits associated with the practice of inference.

Still, one must recognize the fact that by definition, no sampling plan can ensure the acceptance of only perfect shipments. Such assurance can only be achieved through 100% inspection of all incoming items.

One potential way to allow for 100% inspection of all incoming shipments[21] without causing significant delays throughout the supply chain is through the use of item-level RFID. By tagging

[21] As with the proposed statistical sampling, the discussion in this paragraph is limited to inspection based on the product pedigree.

all bottles of medication, it should be possible to automatically read the tags of *all* items included in an incoming shipment and verify their integrity. Such process can be completed quickly, while avoiding the need to open up cases for inspection.

While there are many benefits to such an RFID-based solution, it also requires investment in tags, readers, and more. We therefore recommend decision makers in the pharmaceutical industry to conduct a cost-benefit analysis, to compare the supply chain costs associated with statistical sampling (inspectors' time, training, etc.) with the costs associated with implementing RFID throughout the supply chain, while also taking into consideration the added benefits associated with the ability to scan *all* incoming items. Furthermore, for an RFID solution to be adopted by all business partners, most likely a cost-sharing mechanism will need to be put in place, to avoid a situation in which the manufacturers are the ones to bear the costs associated with tagging all individual bottles, while the downstream supply chain partners are the ones to reap the cost savings associated with the automatic scanning of incoming shipments and lower inspection costs.

About the Stanford Global Supply Chain Management Forum

Housed within the Stanford Graduate School of Business, the Forum brings together faculty and students from multiple schools, departments, and disciplines within Stanford University to manage research projects and disseminate learning. Working with leading thinkers from global companies, the Forum is actively engaged in identifying, researching, developing, and disseminating best practices in supply chain strategy within the context of a dynamic and increasingly global business environment. For more information, please contact Shoshanah Cohen at shosh@stanford.edu.

About the Author

Dr. Barchi Gillai has 14 years of experience in the areas of supply chain management and operations management. Over the years, she successfully completed numerous research projects, many of them in collaboration with Fortune 500 companies and large international organizations. Dr. Gillai has authored several articles, book chapters, white papers, and teaching cases. She earned her Ph.D. in Management Science and Engineering, and her Master's degree in Industrial Engineering and Engineering Management, at Stanford University. She earned her B.Sc. in Industrial Engineering and Management at the Technion – Israel Institute of Technology. Dr. Gillai can be reached at Barchi@stanford.edu.

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Pharma Logic Solutions, LLC (www.pharma-logic.com info@pharma-logic.com) assists Life Sciences, Biologic, Pharmaceutical Distributors, Pharmacies and Healthcare Providers implement solutions and gain business advantages from product traceability, serializations and patient safety.

Projects include solutions involving serialization, track and trace, electronic pedigree (e-Pedigree or epedigree), radio frequency identification (RFID), barcoding and scanning, GS1 electronic product code information services (EPCIS), supply chain, warehousing and EDI.

Strategy, business and user requirements, designs and implementation project have included solutions from multiple vendors.

Vendor selection projects have helped organizations understand how commercial solutions align with the company' unique business practices and compare based on the business requirements.

Projects involving pilots have helped organizations plan, execute and identify areas of a solution that may require refinement before being implemented across the organization' enterprise.

All projects are performed with regulatory validation and requirements, including various country requirements and US Code of Federal Regulations Title 21, part 11, in mind.

Serialization | Traceability | e-Pedigree | Barcodes | RFID | Supply Chain | Packaging | Labeling
Warehousing | Distribution | Strategy | Requirements | Design | Vendor Selection | Pilots

Comments Submitted Re: Inference and Certification of Individual Package Unit

Manufacturers

AMGEN

Amgen Inc.
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August 31, 2012

Executive Officer Virginia Herold
Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

RE: Opportunity to Submit Information Necessary to Possible Board Rulemaking On Inference and Certification of Individual Package Units – Drug Pedigree Law; ISSUE DATE: July 23, 2012

Dear Madam:

Amgen discovers, develops, manufactures, and delivers innovative human therapeutics. A biotechnology pioneer since 1980 headquartered in Thousand Oaks, CA, Amgen was one of the first companies to realize the new science's promise by bringing safe, effective medicines from lab to manufacturing plant to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, bone disease, and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. (For more information, visit www.amgen.com)

Amgen is pleased to be afforded the opportunity to provide comments on the *Opportunity to Submit Information Necessary to Possible Board Rulemaking on Inference and Certification of Individual Package Units – Drug Pedigree Law*. Amgen endorses the Board's commitment to ensuring the safety of patients and the drug supply. Amgen is committing major resources to the implementation of its serialization projects in order to play its part in building an interoperable system. While Amgen has not finalized all of the details of its serialization system, and many aspects of this system are proprietary and confidential, it offers the following comments:

- Aggregation and Inference are critical operational and inventory management elements in making serialization and interoperability a more cost-effective and impactful method to protect patients and the drug supply.
- As part of good manufacturing practices, Amgen actively takes precautions to ensure quality is maintained throughout the production and distribution of goods to our wholesalers and other authorized distributors. For example, our quality management system requires that equipment, information systems, and processes are tested and validated prior to their use for production. Automated verification is also built into the packaging process to confirm correct information is printed on the products and their secondary packaging. Sampling during production is performed to further verify that quality is sustained. Applicable staff are trained on and use standardized procedures where appropriate as part of this quality management system. We intend to use the quality management system to ensure serialization and aggregation attributes, like any other quality attributes, meet Amgen standards and comply with all applicable laws and regulations.
- Amgen recommends that regulators provide guidelines for the use of inference. However, these guidelines should not specify how an aggregation and inference process should be performed or what the acceptance criteria should be. Manufacturers and other supply chain members should be

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allowed to determine how to perform quality checks and establish the appropriate criteria, in line with their existing quality practices.

Again, Amgen wishes to thank the Board of Pharmacy for receiving its comments on the important issue of inference.

Amgen is committed to work proactively with the Board of Pharmacy to enhance regulatory and compliance systems to secure the drug supply chain. We share the Board's concern about the public health impact caused by diversion and counterfeiting and strive to meet our corporate mission of serving every patient, every time.

Sincerely yours,

Lewis T. Kontnik
Director, Brand Protection

APOTEX
ADVANCING GENERICS

August 24, 2012

California State Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento CA 95834

Dear Members of the California Board of Pharmacy,

Apotex welcomes the opportunity to comment on the Board's request for information regarding the pharmaceutical supply chain's use of inference in carrying out the requirements of California's electronic pedigree law. Apotex believes an end-point model would most efficiently achieve the public policy objectives of an electronic track and trace system at the state and/or federal level, and that, under such a model, aggregation and inference would not be necessary. Unlike an end point system, however, California's law requires the tracking and tracing at the unit of sale level. Under any such system requiring confirmation of serial numbers at each movement through the supply chain, it is essential, for efficiency and cost containment purposes, that inference be allowed. Requiring the scan of each unit will increase the cost of pharmaceuticals and introduce significant disruptions in product movement through the supply chain with potentially adverse impact on the public's timely access to affordable medicine. Accordingly, Apotex strongly encourages the California Board of Pharmacy to permit the use of inference under its electronic pedigree law as currently proposed.

Apotex would also like to take the opportunity these comments provide to express its concerns about the ability of the entire supply chain to meet the deadlines for compliance with California's electronic track and trace law. While Apotex will be ready to meet these deadlines, our ongoing preparations leave us with the view that the complexity of the task continues to pose significant challenges for compliance of the supply chain as a whole under the proposed deadlines. For example, there are some concerns that the effort required to establish e-pedigree connections to our customers will not occur in a timely manner to support the established deadlines. It is feared that, the time each connection is expected to take in conjunction with the anticipated last minute rush will leave some customers unable to conduct business under the new law. The sheer number of connections required in the greater supply chain is also a concern. Apotex therefore urges the Board to keep an open mind on the compliance timeline question as the Board continues to participate in the continuing discussions at the federal level about establishing a national system. Should such a system fail to be enacted this year, Apotex would similarly urge the Board to keep an open mind on the compliance timeline in any such discussions the supply chain should raise with the state.

Apotex Corp. 2400 N. Commerce Parkway Suite 400 Weston, FLA 33326
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www.apotex.com

1. Apotex Corporation (Corp) is the US Company that markets the products of Apotex Inc., the largest Canadian-owned manufacturer of prescription drugs. Apotex Inc. sells a portfolio of approximately 300 affordable medicines to 115 countries around the world. Through its sales and marketing offices in Weston, Florida, and operations center in Indianapolis, Indiana, Apotex Corp. is committed to providing safe and affordable generic medicines to the US market.

2. Apotex plans to address e-pedigree requirements via serialization of unit of sale, inner pack, case and pallet utilizing GS1 standard 2D Data matrix barcodes. Given that barcoding is a line of site technology, we plan to utilize inference to allow for aggregation of child serial numbers to parent serial numbers for inner pack, shipper case and pallet aggregation. Aggregation to higher pack formats would be electronically tracked and included in Advanced Ship Notice (ASN) and some Electronic Product Code Information Service (EPCIS) communications.

   Apotex has partnered with industry leading solution providers to ensure appropriate, validated solutions are implemented to support the serialization and aggregation of our product, as well as the internal storage, tracking of serialized product to our customers down in the supply chain using Drug Pedigree Messaging Standard (DPMS) and EPCIS and to allow for tracing from our Third Party Suppliers.

   Apotex is requesting a regulatory allowance for the use of inference from the Board. As described in our response to question 3, Apotex intends to use inference to aggregate child serial numbers for inner pack, shipper case, and pallet aggregation. Although we are not submitting regulatory language at this time, Apotex fully intends to work actively with all stakeholders on efforts to develop such language.

4. As described in the opening paragraph of these comments, Apotex is strongly in favor of the use of inference in any track and trace system that imposes unit-level tracking requirements. . Inference is required to preserve efficiencies in the US Pharmaceutical Supply Chain while minimizing additional operational costs we expect to incur if inference is not permitted.

5. Inference is a mechanism that enables healthcare entities to conduct business in a manner that leverages best practices to meet the challenges associated with the distribution of serialized products. Inference enables the results of transactions conducted at the parent (case) packaging level to be automatically cascaded to all of the contents of that level automatically, without having to scan each individual unit packed within the parent. Apotex feels that inference is but a part of the solution. Combining inference with validated serialization systems and revised Standard Operating Procedures would balance the need for efficiency with the underlying value of security.

If inference and aggregation are not accepted in practice, the US pharmaceutical supply chain would be forced into unit level verification at every exchange of ownership. This would, no doubt, lead to a severe and unacceptable increase in effort to process drugs through the supply chain. Subsequently, it would dramatically increase the potential for delays in patients obtaining much needed medicines. Additionally, in order to attempt to maintain throughput, many of our downstream partners would be forced to expend a significant amount of energy, time and resources, in sum, leading to an increase in costs which would need to be passed to the end consumer.

Since 2D barcoding has become the data carrier of choice for serialized products, line of sight will be required. If inference is not an accepted practice, it would be very costly to the supply chain and ultimately to the consumer. Having to manually scan each unit of sale shipped and received would result in a dramatic increase in man hours and would expect to lead to supply interruptions caused by the added delays at all levels of the supply chain.

It is our opinion that the acceptance of inference adds no additional risk to the security of product while helping to ensure minimal supply disruptions by maintaining a required level of efficiency in the Supply Chain. Utilizing inference would reduce the need for additional manual handling of units which by its nature could lead to unnecessary human error and additional costs incurred as a result of the additional handling.

It is felt that inference allows for balance in the Supply Chain by maintaining efficient delivery of product down to the end consumer while allowing the various partners to stay true to the intent of the legislation to ensure a more secure Supply Chain for the enhanced safety of all Americans.

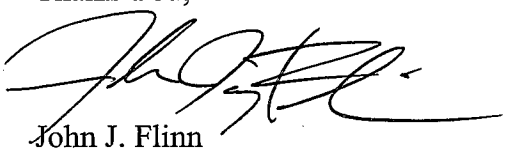
6. Apotex is in the process of finalizing its implementation program. While it is understood this new technology will require changes to Standard Operating Procedures, it is too early to identify the magnitude and specifics of the changes required. We can infer however, that the majority of any SOD changes will be found in the operating of packaging and distribution systems as well as the exchange of information with Third Party partners and customers.

7. Apotex does not feel there should be any allocation of liability. Inference, along with serialization, is intended to provide for an increase in security while minimizing disruption in the pharmaceutical supply chain. Whilst all supply chain partners appear to be working diligently to implement serialization and e-pedigree solutions, we all do so in good faith. In the unlikely event there is a challenge due to inference, we feel this would need to be handled on a case by case basis, allowing for flexibility to resolve the issue at hand. Instituting liability language, in our viewpoint, would undermine the cooperative spirit of the newly secured Supply Chain in the US. Further, it is felt that free market should determine liability, once again, on a case by case basis.

At this time, Apotex would like to take the opportunity to have the Board provide further clarification on grandfathering of existing stock during the transition period. We would also strongly suggest the Board formally support the widely expected use of EPCIS as the primary messaging standard for epedigree. By providing clearer direction on these two critical items the supply chain can focus on implementing the needed systems to support the looming deadlines.

We appreciate the opportunity to provide our perspective on these issues and will continue to work collaboratively with our various trade organizations to support increasing security in our supply chain.

Thank You,



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BAYBIO BIOCOM C·H·I

CALIFORNIA HEALTHCARE INSTITUTE

RECEIVED BY CALIF. BD OF PHARMACY
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August 30, 2012

Virginia Herold
Executive Officer
California Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

Dear Ms. Herold:

The undersigned organizations (BayBio, BIOCOM, and CHI) are California's leading life science associations, representing more than 2,400 biotechnology, pharmaceutical, medical device, diagnostics, research tools, and bioagricultural companies. California is home to the oldest, largest and most productive life science clusters in the world, employing more than 268,000 people statewide. The total economic impact of the life sciences in California is greater than either Hollywood's vaunted entertainment industry or our world renowned wine industry. We appreciate the opportunity to comment on the Board's "Opportunity to Submit Information Necessary to Possible Board Rulemaking on Inference and Certification of Individual Package Units – Drug Pedigree Law" in our role as general representatives for many companies who would be the source point for much of the supply which will enter the system discussed.

Inference is an absolutely critical component to a viable and effective track and trace system. In order to produce a system that does not interrupt and delay the access to medications and other therapies for patients, regulations should encourage use of inference to the maximum extent possible. BayBio, BIOCOM and CHI are concerned that a system without strong utilization of bundling and inference will inevitably create supply stream bottlenecks, delaying the delivery of medications to the consumer and placing great numbers of patients at unnecessary risk. Additionally, it will likely require significant increases in workforce to manage the greatly increased administrative workload. The specific proprietary methods to be used to establish pedigree across our combined memberships will vary, and so we are unable to comment on specific means and methodology to be used by our members. The mere fact that this variance will exist illustrates the complexity faced by our member companies, downstream suppliers, and the Board of Pharmacy in ensuring a fully interoperable system.

Another issue we would like to bring to the Board's attention on behalf of our memberships is that of liability. Manufacturers should not be liable for the actions of those not under their direct control. Once a product has been transferred from the manufacturer's jurisdiction, a manufacturer cannot reasonably be expected to be able to insure or affect its safety and security. Provided all relevant statutes and regulations have been adhered to and packaging is not compromised, liability should follow the product and be conveyed to the parties accepting the product throughout the supply chain. A manufacturer cannot be reasonably held responsible for the actions of downstream participants with whom they have no direct contact or control over independent supply chain actors.

BayBio, BIOCOM and CHI greatly appreciate the opportunity to submit comment in this matter. If we may answer any questions on behalf of our respective associations, please feel free to contact us at the numbers or email addresses below.

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EMD Serono

EMD

Virginia Herold
Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd, Suite N219
Sacramento, CA 95834

August 30, 2012

Dear Board of Pharmacy,

Re: Inference and Certification of Individual Package Units – Drug Pedigree Law

EMD Serono, Inc., the U.S. biopharmaceutical subsidiary of Merck KGaA, Darmstadt, Germany, a global pharmaceutical and chemical group, would like to thank the California Board of Pharmacy for their dedication to protecting the citizens of California though their tireless pursuit of electronic pedigree legislation. Like the California Board of Pharmacy, EMD Serono's goal is to protect patients from unauthentic products and we continue to take an active role in ensuring the safety and integrity of our products.

The industry moves approximately 9 million units per day* making unit level serialization without inference extremely challenging. EMD Serono thanks the California Board of Pharmacy for the opportunity to participate in the creation of practical inference guidelines. As many industry members have stated in previous letters and board meetings, if the industry is required to scan each individual unit throughout the supply chain, the additional burden would be devastating to the industry.

Description of EMD Serono's interest in serialization / inference

In 2002, EMD Serono implemented a secured distribution model including a track and trace program for Serostim® [somatropin for injection], a recombinant human growth hormone. Shipments of Serostim® are restricted to contracted pharmacies that participate in this program. Each Serostim® unit is uniquely serialized and can be tracked to the patient level. In 2003 the FDA stated that the Serostim® tracking program is an effective solution.

Since the California Board of Pharmacy proposed the electronic pedigree and serialization legislation in 2004, EMD Serono has been diligently working on implementing an interoperable system using the GS1 standards and initiating pilot programs with wholesalers. Currently, EMD Serono has two pilot programs underway with two of its three major wholesalers.

EMD Serono

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EMD Serono is an affiliate of
Merck KGaA Darmstadt, Germany.

Description of the means and methodology that have been deployed by EMD Serono

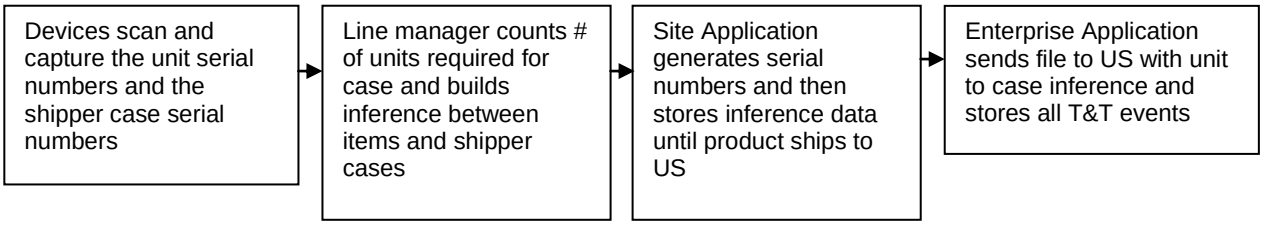
As noted in previous submissions to the California Board of Pharmacy, in order to implement serialization, EMD Serono had to establish a cross-function team including: Supply Chain, IT, Packaging, Manufacturing, Quality Assurance, Regulatory Affairs, Government Affairs, Legal and Procurement. This global team was successful in completing the following projects:

- Packaging modifications to add 2D barcodes and serial numbers,
- An application to capture and track all serial number events,
- State license processing and validation upgrades to include on the ePedigree,
- An upgrade to our 3PL interfaces to capture all data fields required for the ePedigree
- And finally the ePedigree solution.

All projects were completed by 2008 and we continue to make enhancements and phase in serialization. Currently we have eight out of eighteen major products serialized and plan to have all products serialized by 2015. The current system design is made up of four levels.

- Level 1: Devices and Printers
- Level 2: Line Controller
- Level 3: Site Application
- Level 4: Enterprise Application

As you see in the flow below, each level is essential to the serialization process.



Product marking at MFG	Each unit has a 2D barcode with the sGTIN encoded. (In 2015, each unit will have the sGTIN, lot and expiration date encoded into the 2D barcode.)
Data capture and Uniqueness check	Each unit is read immediately before being packaged into the case to ensure the following; 1) There are no duplicate serial numbers 2) The correct serial numbers are placed into the case 3) The correct item serial numbers are aggregated with the correct case serial number

Aggregation file building at MFG	All aggregated unit and case serial numbers are stored in the system as a “manufactured lot”
Product shipped to 3PL	A file with the unit to case association is sent to the 3PL for verification upon receipt.
In-bound at 3PL	Product is received and placed into quarantine until all verifications are complete, including quality and quantity checks.
Out-bound from 3PL	Product is scanned on the outbound, captured and passed via an electronic pedigree to the downstream trading partners.
Other inbound at 3PL	Product which is moved to retain or reject is captured and stored as product that will never ship to trading partners.
Returns	Product returns are captured as returned and sent for destruction. (Redistribution of returns is extremely rare and would need to go through extensive quality checks prior to placing product back to stock.)

EMD Serono has taken a number of steps to ensure the correct serial numbers are placed into the correct case. For example, our system logic will not allow a case to be completed and sealed until the serial numbers match the total case quantity. In addition, our manufacturing sites make sure item serial numbers are only scanned once the items are placed into the shipper case and also ensure the correct case label is applied to the correct shipper case.

Furthermore, our cases are packaged using branded tape. Therefore, any case that has been opened will be apparent. Less than full case quantities will invalidate the case serial number, requiring the case to be opened and all items within scanned individually.

Our final check is with our 3rd party logistics company. Upon arrival the product is placed into quarantine until all necessary quality and quantity checks are complete. For serialized product the quantity is validated against the serialized aggregated file received from the manufacturing site. If there is a discrepancy, each unit is scanned on the inbound to ensure the file is correct prior to shipping product to our trading partners. In addition, we have a final check on the outbound, which ensures there are no duplicate serial numbers within the file.

Reasons that inference is necessary and advantageous

Each supply chain step, starting from the goods outbound from the manufacturing site, requires identification of the shipped or received items. This operation cannot be managed without inference:

Having no inference would mean that every single item should be read/scanned individually, which would represent hundreds of thousands of scanning operations. Not only would this dramatically slow down the goods movements at each node, but it would also significantly increase the risk of error in the scanning operations.

We therefore believe that inference clearly decreases risks of diversion of counterfeiting, and is necessary and advantageous in order to

- Ensure the ability to track all individual serial numbers of a shipment within a reasonable time frame
- Maintain a seamless flow of goods through the supply and distribution chain
- Decrease the risk of error in the code reading operations and thereby minimizing the opportunity of counterfeit product entering the legitimate supply chain.

EMD Serono has taken great strides in serialization and has taken great efforts in ensuring the integrity of case inference. We have system checks, manual checks, clear Standard Operating Procedures and multiple checks prior to shipping product to our trading partners. In addition, in February 2012 our global team kicked off a new project to enhance the systems to reduce manual checks and further streamline the processes for global efficiencies.

As mentioned above, EMD Serono applauds the California Board of Pharmacy and other relevant Federal and State agencies for their continued efforts to ensure that measures remain in place by law to prevent counterfeiting and diversion throughout the United States. We have and will continue to work closely with the Federal and State authorities to ensure that our genuine medicines will reach patients for whom they are intended and will continue to advocate for a national standard. EMD Serono remains committed to assessing, testing and incorporating potential new technological advances in product tracking and distribution as they become practically available.

Date of Submission
August 30, 2012

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* Source: HDMA

RESPONSE TO CALIFORNIA BOARD OF PHARMACY

RE:INFERENCE

Thank you for the opportunity for GPhA to comment on inference and its role in compliance with the California Pedigree Law. The generic pharmaceutical industry is committed to providing safe and effective products to US consumers and believes that maintaining and improving the safety of the US supply chain are important components of achieving that goal.

The Generic Pharmaceutical Association (GPhA) represents manufacturers of generic drugs. Generic medicines now fill 80% of the prescription drugs dispensed in the US yet account for only 25% of the total cost. Over three billion of the four billion units sold in this country are generic. Given the enormous volume, compliance to the California ePedigree law by the mandated dates represents a large, complex and costly challenge to our members.

GPhA understands inference, within the context of the California law, to mean the ability of a downstream partner to infer, or assume, the contents (units) of an aggregate container (i.e., case or pallet) from information provided by the prior owner of the product, without necessarily opening that aggregate container. The ability to infer in this fashion, assumes that the prior owner has done aggregation, or created a parent-child data relationship (between the pallet - case – unit) and passed that data in a pedigree document to a downstream partner. Generic manufacturers are having great difficulty with meeting a certifiable aggregation requirement due to:

- Limits of aggregation technology and applications.
- Cost of aggregation.
- The value of manufacturer aggregation to increasing patient safety through increased supply chain security.
- Difficulties with data integrity and certification.
- Liability of data errors.

Aggregation Technology

The data carrier used by most, if not all, manufacturers planning to comply with California is the 2D barcode. 2D is readily available, has very high reliability and is relatively inexpensive. An interoperable system must enable downstream partners to infer the contents of aggregate containers. Because 2D barcode is a line-of-sight technology, establishing an accurate parent/child relationship between units, cases and pallets (i.e., aggregation) relies on cumbersome, inaccurate and expensive technology.

In a 2D scenario, manufacturer aggregation requires 360 degree visioning systems stationed in front of an automated case packing machine. Each serialized unit is scanned using optical character recognition technology as it is packed into a new case. This process varies from line to line depending on the presence of automated case packers, palletizers, different package types - i.e., tubes, cartons, bottles - which sometimes results in units needing to be turned, tilted or manipulated robotically to allow the

scan of the label at high speeds. Once the appropriate number of units has been packed into a case and that case is sealed, the system at the line level virtually creates that case with those specific units inside. In turn, when cases are stacked onto pallets, the cases typically must be hand-scanned, unless a palletizer is present. That step would complete the aggregation of units to cases, and then cases to pallets. The ability to get accurate scans while operating at production speeds, while also accounting for all of the different misfeeds, sampling for quality assurance, line stoppages, etc., makes this process cumbersome and very expensive. Errors are a certainty, potentially caused by any number of factors from packaging types and shapes, to equipment issues and technology limitations, to line exceptions.

The Value of Manufacturer Aggregation

75%-90% of cases, and virtually 100% of pallets are opened or divided and the units subsequently placed in a new aggregate container by the first supply chain customer, thereby obviating the manufacturers aggregation information for those affected units. The lion's share of generic Rx products are sold through the "big 3" wholesalers. Most of these cases are opened and the units piece-packed at the wholesaler for subsequent sale. The net effect of this repackaging after one "hop" in the supply chain is that units would likely need to be "re-aggregated" to their new containers at the wholesale/distributor stage in order to allow inference further down the supply chain.

Given this value proposition for manufacturers aggregation, it is important to look at the costs:

Costs for Manufacturers Aggregation (Industry estimate)

Assumptions:

- Assumes 2D barcode as data carrier
- This model does not include cost for line shutdowns, re-engineering due to speeds or space constraints.
- This model does not include cost for returns or shipment refusals due to lack of certification, etc.

Number of drug manufacturers serving the US market		425
Number of production / packaging lines - industry aggregate	$	3,250
Typ. Cost per production / packaging line with serialization, but no aggregation	$	125,000
Typ. Cost per production / packaging line with serialization and aggregation	$	750,000
Typ. Cost of Database / EPCIS/ Pedigree and integration	$	2,000,000

	No aggregation	***With aggregation***
Total cost of production / packaging lines	$ 406,250,000	$ 2,437,500,000
Total cost of database and integration	$ 850,000,000	$ 850,000,000
(*One time*) Simple CapEx subtotal	$ 1,256,250,000	$ 3,287,500,000
***Annual* OpEx (Maintenance / Updates)**	$ 251,250,000.0	$ 657,500,000

So, the net value of a $3.3 billion manufacturer investment, and annual maintenance of $658 million in aggregation technology is the transmission of a parent/child relationship for only one step in the supply chain in most cases. GPhA believes that in order to allow the entire supply chain to infer the contents of aggregate containers (cases and pallets), it would be necessary for serialization of the new containers (totes, etc.) plus "re-aggregation" of the units to those totes, increasing the costs detailed above in total industry terms.

Difficulties with Certification Mandates in California's law

An important aspect of California's law is the certification of the accuracy of pedigree information with every change of title in the supply chain. Given the description of the manufacturers aggregation process as detailed above, GPhA believes that it would be very difficult, if not impossible, for a manufacturer to certify aggregation information for 100% of product. The available technology and processes are simply not 100% accurate in scale and at production speeds with different product and package types.

Another complication in the certification aspect of California's law is the common use of third party manufacturers. Under California's law, the ANDA holder in the case of a generic, is the manufacturer, meaning that company must create a certifiable pedigree. In the case of a contract manufacturer relationship, which all of the large generic manufacturers have, much of the industry will be in the position of certifying aggregation information that is not under the manufacturer’s direct control.

Potential Liability for errors in inferred data

GPhA believes that the vision systems currently available for the aggregation of serialized units fall short of 100% reliability. Therefore, a certain percentage of system error is unavoidable for aggregated data regardless of standard operating procedures. Further, manufacturers cannot be held responsible for the operating processes and procedures of other supply chain participants and their handling of data. GPhA urges the board to take this into consideration and establish liability rules only to the company holding title to a product at the time of an incident.

Thank you very much for the opportunity to provide comments on inference. GPhA looks forward to participating in this process with the ultimate goal of an achievable, reliable and cost-effective system which results in a safer supply chain for all.

Johnson & Johnson
WORLDWIDE GOVERNMENT AFFAIRS AND POLICY

August 31, 2012

Virginia Herold, Executive Officer
Board of Pharmacy
1625 N. Market Boulevard
Suite N219
Sacramento, CA 95834

Dear Ms. Herold:

On behalf of the Johnson & Johnson companies affected by the California Drug Pedigree Law, we appreciate the opportunity to provide information to the California Board of Pharmacy on the possible rulemaking on inference and certification of individual package units as it pertains to the California Drug Pedigree Law. Johnson & Johnson is the world's most diverse and largest health care company - actually a family of 250 companies producing pharmaceuticals, biologics, medical device and diagnostics and consumer health products, with operations in 60 countries (including 15 companies in California). Looking at only the pharmaceutical and biologics portions of the company, we are the eighth-largest pharmaceutical company and the fifth-largest biologics company in world.

1. Efforts of Johnson & Johnson Companies.

Johnson & Johnson companies take a variety of approaches to identify and mitigate the risks of counterfeit health care products. They include a range of product and packaging security measures that help distinguish the authentic product from a counterfeit, and aid in minimizing the potential for tampering. Affected companies within the Johnson & Johnson family are working earnestly to be in compliance with the California pedigree law when it becomes effective on January 1, 2015. This involves a significant undertaking to outfit our global packaging network with capability to apply the FDA's Standardized Numerical Identifier (SNI); upgrading our U.S. distribution centers to handle SNI labeled product; working with our external contract manufacturers to ensure they can apply SNI's to products that they manufacture for us; and upgrading our business and IT capabilities to support the new processes. As we are working to implement these capabilities needed to comply with the California pedigree law, we must also ensure that all our processes and systems are GXP compliant and that we maintain uninterrupted patient access to our products.

2. Use of Inference.

Fundamentally, Johnson & Johnson believes that inference is important to maintaining the uninterrupted supply of pharmaceutical products to patients and caregivers. We employ inference when moving product through our supply chain and fulfilling customer orders. Once SNI's have been applied to our products, we intend to maintain the association between the lot number and each individual SNI within that specific lot so that we are able to use inference in our distribution centers when we pick, pack, verify, and ship SNI labeled product to fulfill a customer's order.

We have a number of U.S. customers who distribute product to California-based pharmacies who will need processes and capabilities to exchange SNI's and business event related information. Our intent is to provide information to our trading partners via a system that conforms to GS1's Electronic Product Code Information System (EPCIS) standards.

3. Need for Regulatory Action.

While we fully expect that all legitimate companies interested in continuing to do business in California will seek to comply with the e-pedigree, there are substantial challenges in doing so. As such, it is critical to establish an interoperable electronic system that connects all trading partners and allows for the reliable and efficient exchange of e-pedigree data in order for companies to be able to comply with the CA law. In spite of the efforts being made by the Johnson & Johnson companies, as well as other industry leaders, California's law cannot be successfully implemented unless the Board and the FDA provide guidance and possibly regulations in several areas. These include:

a) Interoperable Electronic System Requirements and Regulations – over the last several years, the Johnson & Johnson companies have worked with the Global Health Exchange (GHX) and several trading partners to understand an option for sharing SNI related information. Although it is very preliminary, our work with GHX demonstrates the challenges with exchanging SNI related information between trading partners. We encourage the Board and the FDA to provide guidance to the industry by publishing regulations that define clearly the expectations for interoperability. Before the stakeholders within the pharmaceutical supply chain can successfully comply with the CA pedigree law, a number of key areas require resolution with respect to interoperability, including the following:

I. Interoperable Electronic System Specifications – Will a single industry solution or will multiple solutions be acceptable? What will be the planned architecture – e.g., centralized, semi-centralized, distributed/de-centralized? What are the data specifications that are required to ensure interoperability across trading partners – e.g., field lengths and formats?

II. Document Pedigree Model System (DPMS) vs. Electronic Product Code Information System (EPCIS) – Can a pedigree on request model using the EPCIS standards be used instead of the document based DPMS? Are physical pedigree documents required? What are the requirements for system availability? Can a pedigree document be electronically generated at the time of the inquiry? Are electronic signatures required to verify the authenticity of a product's pedigree?

III. Management and Accountability for the Interoperable Electronic System – Who is responsible for funding, managing and operating the interoperable system? Who is tasked with running the interoperable system on a day-to-day basis? Who is responsible for data integrity within the interoperable system?

b) **Phased Implementation and Enforcement Discretion** – Since California's pedigree law requires interoperability across the industry, we recommend that the Board formally state that it will exercise its discretion when enforcing the provisions contained across the phases and milestones as defined by the law, until the Board verifies that the majority of supply chain participants can exchange SNI related information.

c) **Liability** – With respect to liability, as stated previously, we intend to make information available through an EPCIS compatible system so that our trading partners can verify our product's SNI and the relevant business event information related to our products. We intend to certify the accuracy of the information related to our outbound shipments, and to certify the authenticity of an SNI on request.

However, we believe that manufacturers should not be held liable and, indeed, cannot be held liable for actions by our downstream participants, and for those participants who do not verify pedigree information. In particular, we should not be held liable to certify to the accuracy of a pedigree once legal title has been transferred to another entity.

We support the comments made in the submission by the Pharmaceutical Research and Manufacturers of America (PhRMA). Specifically, PhRMA's views related to liability and the challenges with achieving a "zero defect system" for the purposes of certification.

Thank you again for the opportunity to provide feedback on the Board's request for information on inference. If you have any questions or comments regarding the points raised in this letter, please feel free to contact me at (510) 248-2362.

Sincerely,

Nancy Noe

Nancy Noe
Manager, State Government Affairs & Policy

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August 31, 2012

Virginia Herold
Executive Officer
California Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

RE: Opportunity to Submit Information Necessary to Possible Board Rulemaking On Inference and Certification of Individual Package Units – Drug Pedigree Law

Dear Ms. Herold:
MERCK & CO., INC. appreciates the opportunity to provide information to the California Board of Pharmacy (the Board) in response to its request for information for a possible Board rulemaking on inference, pursuant to California Business & Professions Code § 4163.3. Merck is fully supportive of appropriate measures to increase supply chain security. The seriousness of pharmaceutical counterfeiting goes well beyond the financial impact that is experienced by other industries. When counterfeit pharmaceuticals are introduced into U.S. commerce, patient safety and confidence in our drug distribution system is compromised and the potential for patient harm, including even death exists. It is for this reason that we continue to believe that a national system should be developed, aligning all states with a system that is both technically viable and will foundationally support further enhancements, if required.

Merck is a global healthcare company working to help the world be well:

- We manufacture and provide innovative medicines, vaccines, biologic therapies and consumer and animal health products to help improve health and well-being;
- We work with customers in 140 countries to deliver broad-based healthcare solutions; and
- We demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships to help people around the world lead healthier lives.

Merck has been actively engaged in standard setting groups such as GS1 and currently co-chairs the National Council for Prescription Drug Programs (NCPDP) work group 17 on product traceability. As a global company, we have also been active in the European Federation of Pharmaceutical Industries and Associations (EFPIA) in the development of the European pharmaceutical authentication system and have successfully deployed serialized product in specific markets based on their requirements.

Merck has performed pilot programs and continues to make significant investments to prepare for the future supply of serialized product to the U.S. market. In fact, some earlier investments, such as in software as an example, may never be utilized since the method to communicate serial numbers has not been fully defined (i.e., DPMS electronic pedigree most aligned with current California law versus EPCIS track and trace aligned with the FDA vision).

Merck is supportive of inference. We believe it is necessary and should be permissible. Today, inference is widely and effectively used throughout the supply chain to ascertain key information (i.e., product, lot number and expiration date) regarding product in sealed, homogenous cases. Another example would be for supply of bulk tablets to off-site packaging operations. In this latter situation, appropriate controls are maintained when Merck fills drums of tablets to assure the identity of the product and the associated lot number are accurate. These sealed drums are then brought to a tablet filler, again through an appropriately controlled environment, allowing inference of the product and lot number in each bottle when packaged.

While we acknowledge the utility of inference, we also recognize its limitations. There are situations in which inference is not accurate enough. For example, the FDA requires that labeling use one-hundred percent electronic verification because using inference would not guarantee that a supply of labels from a supplier is homogeneous and the ramifications of a misbranded lot are serious enough to warrant recalls. Merck performs documented testing to prove the consistent reliability of these systems. This includes operator training, to ensure that each and every alarm is reviewed.

Further, inferring the serial number of each unit associated with each case is different than inference of tablets filled in bottles. First, each packaging line is different. Merck packages prescription drugs in various types of dosage forms, including, blisters, vials, tubes, and bottles - each with its own separate packaging process. Packaging is further complicated by the complexity of equipment, speed of the lines and available space to install new or additional equipment on existing lines, both at Merck facilities and/or at contract facilities. Exceptions in the packaging and distribution processes can have a dramatic impact on case accuracy. For example, if a machine stops, it may cause a change in the normal flow of product on a line impacting case accuracy. In the case of general business processes, the quality unit may sample from a selected case at any time while in our possession. If management of business processes after packaging are not managed correctly, such as the quality sampling example, case accuracy may also be impacted.

In distribution, product is picked into totes that will again have its content inferred. This is currently done for billing purposes and is managed in a similar way that lots are managed. However, transitioning the level of inference from its current use for billing purposes to inferring all serial numbers is a significant leap in technology and business processes for the quantities and varieties of packages required for the State of California.

This is another area that will take substantial efforts to improve if current error rates are not acceptable.

We respectfully submit that the Board considerations, include the level of accuracy required for serial number aggregation and whether that level of accuracy may be achieved through the varying processes within the supply chain. The example often cited by the California Board of Pharmacy is the ability to pick a product on the shelf and establish where it has been. What if this cannot be established because of a glitch in inference? In accordance with 4163.3 (e), what should be the disposition of that product and what supply chain partner should be responsible for the glitch?

Given the concerns regarding accuracy outlined above, Merck is also concerned with how statistical sampling may be applied to the inference process as requested in 4163.3 (d). If one was to use ANSI ASQ Z1.4 2008: Sampling Procedures and Tables for Inspection by Attributes, as an example, there would be a number of variables that all come back to the level of acceptable risk. Developing a sampling plan using this methodology requires understanding confidence limits, acceptable quality levels, lot size and sampling locations. From a manufacturer's perspective, each packaging line would represent a different process having its own unique operating curves. As the Board considers statistical sampling requirements, it should consider what the impact would be if a lot fails statistical evaluation? Would that product be acceptable for sale? Would it put into question other packages within that lot?

With respect to inference upon the effective date, Merck agrees that it:

- **Can** certify that the correct product, lot, and expiration date are aggregated to a sealed, homogeneous case allowing for accurate inference.
- **Can** certify that case and individual unit serial numbers are aggregated to a lot allowing for accurate inference.
- **Can** verify the serial number associated with sealed, homogeneous cases along with its recipient.

However, Merck **Cannot** certify the level of accuracy for individual unit serial numbers being aggregated to a case number. We will require considerable commercial operation, assessment time (not pilot) to fully evaluate every potential cause for variation and to understand the impacts of corrective actions.

Finally, with respect to responsibility, Merck should not be held responsible for downstream participants who do not verify pedigree information. Manufacturers can only reasonably be expected to certify to the accuracy of the information they generate with each outbound shipment, and to, with appropriate security controls in place, certify to the authenticity of particular standardized numerical identifiers, when requested. Once

a product is outside of a manufacturer's control, it is not reasonable or feasible to hold that manufacturer responsible.

In conclusion, Merck appreciates California's efforts to highlight this important national issue. We are committed to doing our part in enhancing supply chain security in a manner consistent with our capability and Merck will work to continually improve that capability. We believe that inference should be allowed based on both process capability and level of acceptable risk. It is critical that, for this system to meet safety objectives, the rule making process takes in all comments and considerations when establishing achievable expectations.

Merck appreciates the Board's leadership in protecting the public and providing us an opportunity to provide input on this important legislation. Please do not hesitate to contact me should you have any questions.

Sincerely,

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Tom McPhillips
Vice President – US Trade Group

Pfizer Inc
235 East 42nd Street, New York, NY 10017
Tel 212 573 3192

August 30, 2012

California State Board of Pharmacy
1625 N. Market Boulevard, Suite N219
Sacramento, CA 95834

Re: Pfizer Inc.'s Submission Regarding Possible Rulemaking on Inference and Certification of Individual Package Units – Drug Pedigree Law (Bus & Prof Code § 4163.3)

To the Members of the California State Board of Pharmacy:

Pfizer Inc respectfully responds to the California State Board of Pharmacy's ("the Board's") invitation to provide written comments regarding inference and certification of individual package units. (Bus. & Prof. Code, § 4034, 4163 et seq.)

As one of the world's leading pharmaceutical manufacturers, Pfizer remains strongly committed to providing patients with safe and effective medications of the highest quality. We share the Board's concern for the risk to patient health posed by counterfeit drugs, and welcome the opportunity to work with the Board and other stakeholders to develop effective mechanisms for preventing the insinuation of counterfeit drug products into the U.S. drug distribution system.

Pfizer believes that counterfeiting issues must be addressed on many fronts, including enhanced business practices, regulatory and legislative solutions, heightened enforcement, and employment of technology.

With this in mind, Pfizer respectfully offers the following comments:

General Comments on Inference

As a general matter, Pfizer believes that a single, federal serialization and traceability law is preferred to the existing patchwork of state pedigree requirements. While Pfizer continues to invest in serialization and works diligently toward compliance with the California pedigree law, we recognize that a phased-implementation approach is necessary. A migration path that begins with implementation of item-level serialization and deployment of the required IT infrastructure is a practical step toward the implementation of an item-level track-and-trace solution. To implement the California requirements, Pfizer strongly supports the need for inference.

The use of inference implies the need for aggregation (associating serialized items to a serialized case, for example) and we believe an item-level track-and-trace solution will require aggregation. Aggregation requires a means to exchange information regarding the aggregated items (the serialized units contained in a serialized case). With respect to the exchange of serialized pedigree information, California's electronic pedigree law requires an interoperable electronic system. As a threshold matter, it must be emphasized that such an interoperable electronic system does not yet exist. As a result, Pfizer recommends the Board work with industry stakeholders, standards bodies, and the U.S. Food and Drug Administration (FDA), to define and enable such an interoperable electronic system on a national basis.

Industry is currently assessing three potential electronic systems or models: centralized, decentralized, and semi-centralized. In this context, "system," is used to mean a network that connects all the necessary stakeholders and provides a means for the secure, reliable, timely and cost-effective exchange of information. The nature of the ultimate "system" design and data requirements will impact the need for inference as well as the associated rules.

Since 2005, Pfizer has been working with industry stakeholders, solution providers and standards bodies to deploy and test our serialization capabilities, including our ability to aggregate individual serialized items to higher levels of logistical units (item to cases and cases to pallets) and to successfully exchange the associated data with our trading partners. We have implemented a drug pedigree messaging standard (DPMS) solution and are currently testing an EPCIS "event-based" pedigree model.

In order to align ourselves with where we believe industry is trending, Pfizer has recently made a decision to utilize 2D bar codes going forward as the primary data carrier for serialization, with linear and/or human readable back-up when possible. Pfizer's decision to use 2D bar codes is globally harmonized with initiatives in the EU and elsewhere; it is also aligned with the direction many other pharmaceutical manufacturers are pursuing in the U.S.
The use of 2D technology and the California requirement for item-level tracking necessarily requires the use of inference, given that it is not practical or advisable for others in the supply chain to open sealed cases from the manufacturer for the sole purpose of the confirming serial numbers. In fact, to require sealed manufacturer's cases be opened to scan serial numbers would destroy tamper evident tape and other features designed to alert supply chain participants to potential issues with the package. Indeed, opening cases that are outside the manufacturers' control, as a normal course of business, would increase supply chain risk by increasing the opportunity for theft, diversion and tampering that would then go unnoticed as opening and resealing cases would become common place.

Pedigree Certification

With respect to pedigree certification, based on our pilot experience, we believe unavoidable aggregation errors will sometimes occur, especially in the early stages of adoption of an item-level track-and-trace system. We also believe that other

mistakes are likely to occur, such as shipping errors and master data management issues. As a result, the Board should allow for reasonable accommodations to be made for these situations.

For example, the Board should recognize that if a rigid certification requirement is mandated, which does not allow for exceptions or unintentional errors, the inability to provide an unrestricted certification will likely impede the flow of goods.The inability to resolve these unavoidable errors and exceptions in a timely manner due to strict certification requirements, may impede the flow of goods and prevent them from reaching patients when needed.

Allocation of Liability

Concerning the allocation of liability that may be incurred due to the use of inference, Pfizer believes that provisions or allowance should be made in the Board's rulemaking process to distinguish between unintentional shipping or technology/data errors and intentional misrepresentations of information for the purpose of introducing counterfeit or diverted product into the legitimate supply chain.More specifically, it would be unreasonable to expect that there will never be inadvertent or unintentional errors with physical shipments, whose errors are then captured in a pedigree. It is our belief that the intent of the California law is not to prosecute individuals or organizations for unintentional shipping errors. Nor, do we believe the unintended consequence of unnecessary delays in the delivery of important medications to patients should be permitted as a result of unintentional shipping errors.

As a result, the requirements for certification relating to pedigrees should reflect this reality and provide that inadvertent and unintentional errors would not render a certification to be considered false. Further, at best, any entity within the supply chain can only certify as to the information that such entity provides. Entities should not be liable for the accuracy of information that the entity cannot itself verify, e.g., information supplied by participants further down the supply chain. This should be clarified through the rulemaking process.

Regarding liability associated with the accuracy of pedigree information using inference, we believe the Board should clarify that provided there are processes and procedures in place to ensure a reasonable degree of accuracy with respect to information contained in a pedigree based on the use of inference, no liability should flow from the reasonable and intended use of inference. To the extent any liability should be associated with the accuracy of pedigree information, it should be determined based on the intentional misrepresentation of information.

Conclusion

Finally, Pfizer supports the use of inference and believes it should be permissible in an item-level track-and-trace system. In fact, given the industry movement toward adoption of 2D bar code technology, we believe the use of inference is a necessity. We are committed to working with the California Board of Pharmacy, the FDA and other industry stakeholders to develop the requirements around its use. However, before the inference rules can be written, additional details about the item-level track-

and-trace system to be utilized are needed. There should be a better understanding of the complete process, including the system architecture and data requirements and how exceptions will be resolved in order to inform decisions around inference rules. For example, whether an item was read or "inferred" upon receipt will impact how an exception is resolved. The entire process is inextricably linked and must be defined before Inference rules can be determined.

Pfizer is committed to working with the Board, GS1, and others to further assess various system architecture models (the GS1 network centric e-pedigree models) and to address exception handling issues. We are actively engaged at this time in the work being done by GS1 Healthcare US to address the resolution of exceptions and in documenting findings from our pilot activities in the GS1 Implementation Guide, "Applying GS1 Standards to U.S. Pharmaceutical Supply Chain Business Processes". We look forward to sharing this work with the Board when complete.

Pfizer appreciates the opportunity to provide this input to the Board and looks forward to working with you in the future. Please contact me at (212) 573-3192 if you have any questions.

Sincerely,

Tom McPhillips
Vice President
US Trade Group

PhRMA

August 28, 2012

Virginia Herold
Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

Re: Use of Inference

Dear Ms. Herold:

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to provide information to the California Board of Pharmacy (the Board) in response to its request for information for a possible Board rulemaking on inference, pursuant to California Business & Professions Code § 4163.3. PhRMA represents the country's leading innovative biopharmaceutical companies, who operate globally. PhRMA member companies are committed to researching and developing new medicines to help patients live longer, healthier lives.

While PhRMA recognizes that the Board specifically requested input on inference, the Board's request for information touches on key aspects of an interoperable electronic pedigree system that must first be defined, in order to fully evaluate inference. PhRMA also continues to believe that a national system is preferable to any one state system. Nonetheless, we remain committed to helping California implement its law, and encourage the Board to define the data elements, system architecture, and other infrastructure necessary to achieve an interoperable electronic system.

Since California amended its law in 2008, PhRMA members have engaged in a number of pilot activities and have learned a great deal about data exchange and the elements and steps necessary to achieve an interoperable electronic pedigree system. The pilot work completed to date suggests that an item-level track and trace system as envisioned under California law is not the most effective electronic system to prevent diversion and counterfeiting of finished pharmaceutical products in the finished product distribution chain. The only known way to currently achieve an item level track and trace model is to use the Drug Pedigree Messaging Standard (DPMS). However, the pilots conducted to date suggest that the DPMS model

introduces unrealistic supply chain risks because it requires a high degree of accuracy that has not been proven in pilot work conducted.

More precisely, in order for any electronic pedigree system to function as intended, the pedigree information must be exchanged electronically between trading partners, and these electronic data exchanges must match the physical flow of the product. Both pieces must work together to allow uninterrupted movement of pharmaceuticals through the distribution chain. However, the pilot experiences with DPMS to date demonstrate that when exceptions or errors in the data exchange occur, the physical flow of the product stops. PhRMA members are greatly concerned about the cumulative impact of this phenomenon on the ability of patients to obtain their medicine. If, when the system envisioned in California is fully operational, exceptions or errors in data exchange halt the further distribution of products, this will have a negative impact on product supply and patient care. And, the cumulative effect of these errors will have a ripple effect throughout the distribution chain.

The pilot work conducted to date has also involved distributed database models. PhRMA members believe that pilots of other database models, to assess both patient access and product protection, are necessary, and we are willing to work with the Board and others to conduct such pilots.

Notwithstanding this fact, PhRMA members remain committed to helping the state implement its law. As such, PhRMA members are beginning to serialize products at the item level, and to create databases containing information about those products at the item level that will allow for downstream supply chain participants to authenticate or verify those item numbers. These activities will facilitate the exchange of item level information in the supply chain, but they do not lead to the creation of an interoperable electronic system required under California law. Thus, this is where the Board must exercise its leadership to develop such an interoperable system.

Given that it's unclear what type of interoperable pedigree system will be developed nationwide or in California, developing regulations on inference at this time could be premature. Manufacturers need to know what type of interoperable system will be established to enable supply chain participants to meet the state's interoperable pedigree requirements. Will California establish a centralized system, a semi-centralized system, or a de-centralized system? As stated above, pilot work completed to date have only tested the distributed or de-centralized model.

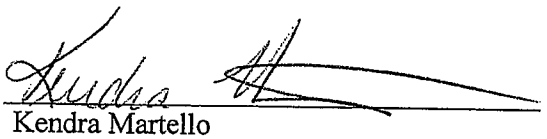
Moreover, under California law, the exchange of pedigree information throughout the distribution chain is not complete until 2017. As downstream supply chain participants begin to receive and exchange pedigree information, a host of unanticipated outcomes that can't be predicted today should be expected. A "detailed description of the means and methodology, including hardware and software specifications, processes, and data carrier(s), that the submitting party has deployed or intends to deploy," is not possible today. Moreover, hardware and software specifications, processes, means and methodologies cannot be known today as they likely haven't been built, and once designed, built, and tested, will be modified and adopted over time.

No matter what interoperable electronic system is ultimately adopted, PhRMA members believe inference is necessary and should be permissible. To manufacturers, "inference" consists of one or more steps that allow a person to infer the contents of a collection of containers as it moves through the supply chain, without having to separately verify each unit or item within the individual collection. As the Board considers these issues, a GS1 document from May 2010 entitled, "The Practice of Inference in the Pharmaceutical Supply Chain," could be helpful to the Board. As product flows through the supply chain, homogenous cases from a manufacturer are broken down and further distributed into secondary packages and containers. In fact, manufacturers believe that very few of their original packaging configurations remain intact throughout the supply chain to a dispensing location. The Board will need to understand the impact of these activities on the use of inference and on product supply and patient access to medicines. Additionally, standard operating procedures (SOPs) to accomplish inference do not presently exist within many manufacturers.

Finally, with respect to liability, manufacturers should not be liable for downstream participants who do not verify pedigree information. Further, the California law requires a certification that the information contained in a pedigree is true and accurate. As the Board considers issues around certification and liability, it should consider the appropriateness of requiring such certifications in each instance. For example, how can an entity certify to the accuracy of a pedigree once legal title to the product has transferred to another entity? This is especially true in the case of returns, which must be documented on the same pedigree as the original transaction. Manufacturers can only reasonably be expected to certify to the accuracy of the information they generate with each outbound shipment, and to, with appropriate security controls in place, certify to the authenticity of a particular standardized numerical identifier when requested. Manufacturers generally understand that achieving a zero defect system may not be expected for the purposes of certification, and that business rules may be used to manage exceptions.

Thank you again for the opportunity to provide input into the Board's request for information on inference. Should you have any questions or comments regarding the issues raised in this letter, please feel free to contact me at 202-835-3549.

Sincerely,



Kendra Martello
Assistant General Counsel

Comments Submitted Re: Inference and Certification of Individual Package Unit

Wholesalers

CardinalHealth

VIA EMAIL (Virginia.Herold@dca.ca.gov)

September 6, 2012

Virginia Herold, Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

Re: Opportunity to Submit Information Necessary to Possible Board Rulemaking on Inference and Certification of Individual Package Units – Drug Pedigree Law (July 23, 2012)

Dear Ms. Herold:

Please accept this letter as Cardinal Health's response to the Board of Pharmacy's Opportunity to Submit Information Necessary to Possible Board Rulemaking On Inference and Certification of Individual Package Units – Drug Pedigree Law, published July 23, 2012. Headquartered in Dublin, Ohio, Cardinal Health helps pharmacies, hospitals, ambulatory surgery centers and physician offices focus on patient care while reducing costs, enhancing efficiency, and improving quality. Cardinal Health is an essential link in the health care supply chain, providing pharmaceuticals and medical products to more than 60,000 locations each day. The ability to use inference in meeting the obligations under the California pedigree law will be a critical process in maintaining efficiency for Cardinal Health and our customers.

Overview of California pharmaceutical distribution business

Cardinal Health has two pharmaceutical distribution centers in California. Our locations in Elk Grove and Valencia service over 3,000 customers; providing pharmacies, hospitals, ambulatory surgery centers and physician's offices with access to over 57,000 items including 20,000 prescription (dangerous) drugs.

The below statistics highlight the approximate volume of annual operational activities for our two California pharmaceutical distribution centers. These numbers illustrate the magnitude of serial number management that will be required for compliance with California pedigree law:

- Receipts: 55 million pieces; 2 million cases
- Shipments: 55 million pieces (75% of which are Rx) contained within 4 million totes
- Returns: 3% of pieces originally shipped

Cardinal Health has been engaged in pilot activities to support implementation of the California pedigree law for more than five years. One of our California distribution centers is currently engaged in pilot activities with several drug manufacturers to build effective controls to comply with the law while ensuring business efficiencies.

Inference definition

Inference can be defined as a conclusion drawn from evidence or reasoning. For the purposes of pedigree, inference is a process that supply chain partners use to electronically match expected receipts and shipments with the physical product actually received or shipped without physically reading each unique serial number within a packaging unit.

Cardinal Health believes that inference, when used responsibly in the receiving and shipping processes, will support efficient operations and will not increase the risk of diversion or counterfeiting within the pharmaceutical supply chain.

Circumstances where inference is necessary

California pedigree law evidences the legislative intent in statute. The Legislature intended that all participants in the supply chain "verify and validate the delivery and receipt of dangerous drugs against those [electronic] pedigrees at the unit level, in a manner that maintains the integrity of the pedigree system without an unacceptable increase in the risk of diversion or counterfeiting." See B&PC §4163.3(a). Inference is an essential operational process that must be allowed in order to comply with the law. The Legislature recognizes this as they included §4163.3(b) the requirement that the Board of Pharmacy, by regulation, shall "define the circumstances under which participants in the distribution chain may infer…". See §4163.3(b). To aid the Board in drafting those regulations, the following circumstances are those which Cardinal Health would like to utilize inference:

- Distributor's receipt of sealed full case(s) when electronic data has been received from the supplier prior to receipt of the physical product. The electronic data received must provide the unit to case relationship.
- Distributor's receipt of full pallet(s) when electronic data has been received from the supplier prior to the receipt of the physical product. The electronic data received must provide the unit to case and case to pallet relationship.
- Distributor's shipment of sealed full case quantities when electronic data has been delivered, prior to the recipient's receipt of the physical product, from the distributor. The electronic data much provide the recipient with unit to case relationship.
- Inference shall not be allowed on receipt of a product through the returns process.

Cardinal Health requests that the Board of Pharmacy draft regulations allowing inference in these above circumstances.

Because Cardinal Health strives to fulfill customers' needs immediately, we ship daily (sometimes twice daily) to customers. These order quantities tend to be single units. Data over a one year period for six serialized NDCs shows that although 70% of products were received

during this period with inference, 98% of units (serial numbers on an individual unit) shipped were physically read upon receipt, shipment, or both. The 2% of units not scanned at the unit level are scanned at the case level. Both receipt and shipment serial numbers for these case level scans are recorded as transferring ownership based on verification of the original electronic transmission provided by the supplier. See chart below for actual pilot statistics in 2011:

Receipt Data

Shipment Data

Procedures to use inference

Cardinal Health has established documented procedures in our distribution center engaged in pedigree pilot activities. Although these procedures may be revised with increased product volume, the major components of the procedures will remain the same and are as follows:

- Supplier must provide electronic transmission via AS2 secured transaction (using either a serialized Advanced Ship Notice, DPMS pedigree, or EPCIS transaction) that provides hierarchy for serialized products
- Procedures are defined to determine which suppliers can be trusted to provide accurate and complete data:
  - Physical verification of a defined number of consecutive receipts
  - 100% match of electronic transmission with physical serial numbers received
  - No manual intervention other than product scans
  - Approval of trusted status by local compliance manager
  - Signed documentation of process compliance
- Random audits performed to ensure ongoing accuracy of electronic transmissions
  - Conducted according to ANSI/ASQZ1.4-2008, using Special Level S-1 and the single sampling plan for normal inspections

Safety of inference

Prescription drug manufacturers have overt and covert methods for securing their products. One of the overt methods is the case seal or tape. The security of the case is compromised when that seal is broken and product continues to move in its original carton through the supply chain. California regulation requires that all materials be examined upon receipt or before shipment. See CCR 1780(d). Our distribution centers examine product to ensure there is no evidence of tampering, such as a broken seal on a manufacturer's case. The ability to infer the contents and leave the cases sealed either until the entire case is sold or until a single unit is needed for a customer, would create a more secure supply chain.

Operationally, inference is preferred because opening every case in an effort to read the individual units would have a significant negative impact on productivity and may lead to overall increased cost to distribute in California. In addition, the use of inference expedites the receiving process, resulting in product being readily available to ship to dispensers that have patients in need of those prescription drugs.

Liability

Each trading partner should be responsible for information they represent as true and for the consequences that result if such information is found to be false or erroneous. Consideration should be given to whether the error was intentional or due to human error or mistake, as well as the seriousness of the resulting consequence.

Parties should be liable for their own actions, but mitigating factors such as properly vetting trading partners, due diligence, long-standing relationships, and past experience (good or bad) with a certain entities should be taken into consideration when determining any liability resulting from reliance on inference as a result of manufacturer provided product and shipment information.

Conclusion

The safety and security of our nation's pharmaceutical supply is one of Cardinal Health's top priorities. We take this responsibility very seriously, as a safe and reliable drug supply is central to our customers' business and critical to the health and well being of patients. We are committed to complying with pedigree laws, including serialization requirements, in the most efficient manner possible. If you have any further questions, please do not hesitate to contact us.

Sincerely,

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Healthcare Distribution Management Association

August 30, 2012

Virginia Herold
Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

Re: Opportunity to Submit Information Necessary to Possible Board Rulemaking on Inference and Certification of Individual Package Units – Drug Pedigree Law (July 23, 2012)

Dear Ms. Herold:

On behalf of the Healthcare Distribution Management Association (HDMA) and its members serving California, I appreciate the opportunity to respond to the Board of Pharmacy's request for comments regarding inference and its use in the context of California's electronic pedigree law. The framework set forth by this law will result in operational and technological changes unlike any the industry has experienced to date. Inference will be an integral part of any implementation strategy for pharmaceutical distributors, and its allowance by the Board is necessary for distributors to meet the goals and requirements of the California law.

HDMA is the national association representing primary healthcare distributors, the vital link between the nation's pharmaceutical manufacturers and healthcare providers. Nearly 90 percent of the prescription drugs in the U.S. are stored, managed, and delivered by our primary distributor members. Every day, HDMA member companies collectively ensure that nearly 9 million prescription medicines and healthcare products are delivered safely and efficiently to nearly 200,000 pharmacies, hospitals, long-term care facilities, clinics and others nationwide. In California, our members serve over 32,000 customers.

We appreciate and support the Board of Pharmacy's request for comments from individual companies. As you know, HDMA also has been significantly involved in the development of the California pedigree law and offers a unique and critical viewpoint on implementation. We hope that this perspective is helpful to the Board as it moves toward 2015 and beyond.

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Background

Inference in the context of electronic pedigree and track-and-trace has essentially the same meaning as it does in the English language – an assumption that a proposition is true based on the occurrence of some other fact or assumption. For example, Wholesale Distributor XYZ received ten individual units in a sealed case (A) from the manufacturer of a product, along with a communication stating that these ten units were numbered 1 through 10 in case A. Because the manufacturer provided this information, and the same manufacturer sent Wholesale Distributor XYZ the case, XYZ can *infer* that what the manufacturer sent to it is what was stated by the manufacturer – without requiring Wholesale Distributor XYZ to open the case to confirm.

The concept of inference first emerged in discussions among pharmaceutical supply chain partners approximately five years ago, when the current iteration of the California pedigree law was being drafted by the Legislature. Historically, California's law has been silent on the specific type of technology and/or data carrier required to satisfy the provisions of the law, but the concept of unit level track-and-trace was based originally on the capabilities of radiofrequency identification (RFID) technologies. In 2007 or 2008, it became clear that manufacturers overwhelmingly believed that unit level serialization was more practical and economically feasible through the use of two dimensional (2D) data matrix bar codes. Because 2D bar codes utilize "line of sight" technology, an individual must scan each bar code in order to capture product information.

On an average day, a typical HDMA member distribution center handles almost 2,000 customer orders, and picks (or processes) an average of 95,000 product units. Due to this high volume and the associated need for efficiencies of scale, scanning individual units on receipt is not always practical or economically feasible. The Legislature understood the need for supply chain members to avoid having to unnecessarily open every single case of product.

In recognition of this concern, the Legislature's solution was the allowance for inference as described in California Bus. & Prof. Code § 4163.3. HDMA reads the statutory language regarding inference as requiring the Board of Pharmacy to issue regulations that define circumstances in which inference may be used. The need for inference still exists today, and without it, primary distributors will have incredible difficulty with implementation, potentially slowing movement of product and bringing the distribution chain to a halt in California.

Below are HDMA's responses to a number of the Board of Pharmacy's specific requests for information.

I. Process and Technology Recommendations

HDMA and its members have been working on implementation issues related to California's pedigree law since before the 2008 law was enacted. Our members have engaged staff and

outside consultants in exploring existing and developing technology solutions in order to help them comply with the California law. Some members have also engaged in pilot programs that will help inform more specific solutions and data exchange between trading partners.

In addition, HDMA members have been participating in the development of GS1 standards and piloting use of those standards. Significant efforts have been put forth and progress has been made; though, there is still more work to be done before the standards are complete and ready for application throughout the supply chain.

It should be noted, however, that the ability of HDMA primary distributor members to comply with the California law is heavily dependent upon manufacturer compliance beginning in January 2016. A future that includes serialized product, use of track-and-trace technologies, and electronic pedigree data exchange is one that has been contemplated, but we cannot yet fully understand or anticipate how such changes will require modifications to our members' operational and logistics functions.

The impact of these changes extends beyond the boundaries of the state's day-to-day product demands, affecting the ability to move product within complex, national, distribution networks, and creating a need for new contingencies for moving product into the state during times of emergency or shortage. Without a critical mass of serialized product entering the supply chain, with unit-to-case aggregated product information (individual SNIs associated to case), distributors will have significant difficulty maintaining their current levels of efficiency, which may adversely affect the availability of drug products in California.

II. Circumstances In Which Inference is Necessary

As primary distributors, HDMA members will be receiving the vast majority of product shipments directly from manufacturers. HDMA believes that inference would be appropriate and should be permitted under the following circumstances:

1) Recipient places an order for product with the shipper, with whom the recipient has a business relationship; and
2) A sealed homogenous (same lot, same product) case is sent by the shipper directly to the recipient; and
3) The shipper and recipient have technology solutions to provide electronic business-to-business transactional security; and
4) The shipper sends – in advance of, or in conjunction with shipment – information about the items/contents of such case, including the items' serial numbers and pedigree information related to each specific case; and
5) The recipient receives the case and the product information from the shipper.

Although the frequency of receiving sealed homogenous cases as described above may vary depending on the manufacturer, product and customer orders, we anticipate that the vast majority of inbound shipments received by primary distributors consist of sealed homogeneous cases.

Please note that most individual units received by primary distributors using case inference will in fact be scanned individually as the units are prepared for shipment to the pharmacy setting. Exceptions to this procedure will occur when distributors ship to large volume customers, such as mail order pharmacies, regional or national pharmacy warehouses, warehousing health systems, or government agencies.

III. Safety Benefits / Advantage to Allowing Inference

Allowing inference by distributors as described above would help to facilitate implementation of the provisions of California's pedigree law. Most important, inference will enable compliance with the spirit and the intent of the law – to employ technology and processes in the supply chain to permit electronic track-and-trace for the first time. Simply put, without inference, such technologies and processes might not be successfully deployed. The use of inference by distributors will help to ensure that California providers and patients have continued access to life saving medicines, while increasing the security of the supply chain. It is anticipated that adoption of track-and-trace and electronic pedigree will create new procedural and logistical burdens for distributors; however, the allowance of inference will at least enable some efficiencies to be maintained.

Successful deployment of electronic track-and-trace technologies and processes is expected to decrease the risk of counterfeiting and diversion within the supply chain. As to the benefit of inference specifically, the use of inference in distribution centers will limit the number of open cases in a warehouse or on a receiving platform, thereby limiting the number of personnel handling product, and thus creating fewer opportunities for diversion, theft or contamination. If the scope of permitted inference is limited as described in section II above, HDMA does not believe that inference would be disadvantageous or introduce unacceptable increases in risk.

IV. SOPs and Statistical Sampling

As a preliminary matter, it is important to note that the statute does not require the Board to promulgate regulations addressing the content of Standard Operating Procedures (SOPs) covering the use of inference. The spirit of the governing statutory provision was to require each company to develop a compliance plan and SOP language compatible with its own processes and implementation plan.

HDMA believes that each individual company opting to use inference should have the flexibility to tailor SOPs to its specific operations, while making such SOPs available to the Board of Pharmacy for review upon request.

If the Board believes that it is necessary to provide greater uniformity among supply chain members in their SOP development, HDMA suggests that the Board limit its guidance to several *general* factors or categories that could be considered in developing appropriate SOPs.

V. Allocation of Liability

HDMA suggests that each trading partner should be liable for the information that they introduce into the marketplace and for the actions/consequences that result if such information is found to be false or erroneous. Further, when assessing liability, the Board should consider whether the error was made with intent or due to mistake as well as the seriousness of the resulting consequence. (e.g., different treatment by the Board for systems malfunctions than for an intentional falsification or negligent assertion.)

For example, in the instance of a manufacturer stating that specific serialized items are shipped to a distributor, labeled with serial numbers 1-20 and contained in a manufacturer's sealed homogenous case, the manufacturer should bear responsibility for the accuracy of that information. For its part, the distributor should be responsible for complying with the state's requirements (including having appropriate SOPs), but the distributor should be able to rely on the information and assertions made by manufacturer, and should be held liable only for violations within its control.

In other words, parties should be liable for their own actions, but mitigating factors such as properly vetting trading partners, due diligence, long-standing relationships or experience with certain entities should be taken into consideration when determining any liability resulting from reliance on inference as a result of manufacturer-provided product and shipment information.

Conclusion

HDMA respectfully submits the above comments in response to the Board's request. The use of inference does not reduce the integrity of the pedigree system nor does it create an increase in the risk of diversion or counterfeiting. As we have stated, inference is a necessary part of implementation of California's pedigree law for distributors, as we expect manufacturers to be employing 2D bar codes to meet their serialization requirements. Without the ability to infer the contents of sealed homogenous cases based on information supplied about the products shipped within those cases, distributors would have severe difficulties complying with the requirements of California's pedigree law.

Please contact me should you have any questions or need additional information. HDMA appreciates this opportunity to provide input and we look forward to working with you on this important issue.

Sincerely,

Elizabeth A. Gallenagh
Vice President, Government Affairs & General Counsel
Healthcare Distribution Management Association

HEALTH INDUSTRY DISTRIBUTORS ASSOCIATION

August 29, 2012

Executive Officer Virginia Herold
California State Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, California 95834

Re: §4163.3. Legislative Intent; maintaining integrity of pedigree system; use of inference

Dear Ms. Herold:

On behalf of the Health Industry Distributors Association (HIDA), I am submitting information necessary to possible rulemaking on inference and certification of individual package units as related to the California drug pedigree law. We respectfully request that the California State Board of Pharmacy (the Board) allow through regulation for supply chain trading partners to infer the contents of sealed containers from an associated serialized numerical identifier (SNI).

HIDA is the professional trade association that represents the interests of over 600 medical-surgical products distributor companies operating throughout the United States. Our members deliver life-saving healthcare products to more than 290,000 points of care including over 210,240 physician offices, 6,512 hospitals, 44,061 assisted living and nursing homes and 33,722 medical facilities. While our members primarily carry medical-surgical products they may also deliver low-risk, high-volume pharmaceutical products used in everyday medical interactions, such as topical anesthetics and flu vaccines.

As the implementation of the California electronic pedigree law approaches, a variety of HIDA distributor members have been challenged with establishing the definitive means and methodology needed to "verify and validate the delivery and receipt of dangerous drugs against electronic pedigrees at the unit level." Specifically, the deployment of hardware, software, and processes associated with these functions (that is, verification, validation, and certification of dangerous drugs at the unit level) is difficult until more guidance is available from supply chain partners and the Board regarding compliance requirements. For example, the scope of a regulatory allowance for the use of inference for the purposes of certification of individual units of drug products will influence certain wholesaler decisions.

Regulatory allowance for inference is a necessity for wholesale distributors to maintain the efficiency of the supply chain. The prevalence of two-dimensional (2D) barcodes as the carrier technology for serial numbers, for example, will require "line-of-sight" scanning capabilities on the part of wholesale distributors to validate serialized numerical identifiers (SNI) on individual units. Opening sealed containers and scanning individual units to validate the contents of each and every container will add significant costs in labor, technology, and time to the supply chain. As such, inference should be allowed for supply chain participants in the following circumstances:

- Upon the receipt of product in a sealed container (e.g., pallet, case, package) with an associated SNI; and

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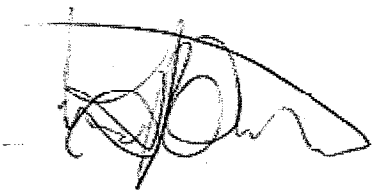
Phone: (703) 549-4432 • Fax: (703) 549-6495 • www.HIDA.org

- Upon the sale of product when the container's seal remains intact and when the contents within a container remain sealed with an associated SNI (e.g., a sealed case contained within a pallet).

Ensuring patient safety remains the priority of medical-surgical products distributors and the use of inference can be used toward that end. By preserving the original seal of a container, and in some cases tamper-evident packaging, downstream trading partners are provided an additional mechanism for assuring the contents are not illegitimate product.

Thank you for the opportunity to submit information on the need for inference in the healthcare supply chain. Please contact Ashley Palmer, palmer@HIDA.org or (703) 838-6113, if you have any questions regarding HIDA's comments to the Board.

Sincerely,



Linda Rouse O'Neill
Vice President, Government Affairs
Health Industry Distributors Association

McKesson Corporation
One Post Street
San Francisco, CA 94104-5296

Ann Richardson Berkey
Senior Vice President, Public Affairs

MCKESSON

September 1, 2012

Ms. Virginia Herold
Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd., Suite N219
Sacramento, CA 95834

Re: Opportunity to Submit Information Necessary to Possible Board Rulemaking on Inference and Certification of Individual Package Units – Drug Pedigree Law (July 23, 2012)

Dear Ms. Herold:

On behalf of McKesson Corporation ("McKesson"), I appreciate the opportunity to respond to the State of California's Board of Pharmacy ("Board") request for comments regarding inference and its use in the context of California's electronic pedigree law.

For 179 years, McKesson has led the industry in the delivery of medicines and healthcare products to drug stores. Today, a Fortune 14 corporation, we deliver vital medicines, medical supplies, care management services, automation, and health information technology solutions that touch the lives of over 100 million patients in healthcare settings that include more than 25,000 retail pharmacies, 5,000 hospitals, 200,000 physician practices, and over 10,000 extended care facilities and 700 home care agencies. McKesson delivers medicines to the entire Department of Veterans Affairs system, as well as to a significant number of Department of Defense and other government facilities. McKesson is also one of the nation's largest distributors of biotechnology and specialty pharmaceutical products and services for providers and patients.

Based on our expertise in pharmaceutical distribution and our history of providing recommendations to the Food and Drug Administration and selected states on technologies and standards to further secure the drug supply chain, we are pleased to provide comments on inference relative to the California drug pedigree law.

Below are responses to the information needed for possible Board rulemaking.

1. **Identifying and contact information for the submitting person or entity.**
   Mr. Ron Bone, Senior Vice President, Distribution Operations, McKesson Pharmaceutical at 415-983-7613 or ron.bone@mckesson.com

   Mrs. Ann Richardson Berkey, Senior Vice President, Public Affairs, McKesson at 415-983-8494 or ann.berkey@mckesson.com

2. **A description of the submitting party's interest in this subject, including the submitting party's role, if any, in the supply chain (e.g., manufacturer, repackager, distributor, or dispenser) or other basis for interest (e.g., vendor, consultant, standards body) and a brief description of the person, company, or other entity responsible for the submission.**

   McKesson is a national pharmaceutical and medical supply wholesale distributor with two pharmaceutical distribution centers and two medical-surgical distribution centers located in the state of California. We have two pharmaceutical supply distribution centers located in Denver, CO and Olive Branch, MS which supply these California facilities.

   Mr. Ron Bone has represented McKesson in GS1 Standards and Traceability standard setting efforts for the past eight years and has been participating regularly in federal and state discussions regarding serialization, traceability and pedigree.

3. **If the submitting party is a supply chain participant, a detailed description of the means and methodology, including hardware and software specifications, processes, and data carrier(s), that the submitting party has deployed or intends to deploy to "verify and validate the delivery and receipt of dangerous drugs against [electronic] pedigrees at the unit level," including specification of the means and methodology for certification.**

   McKesson seeks to protect the integrity of the pharmaceutical supply chain while ensuring the delivery of safe medicines to patients. We scrutinize our trading partners and hold trusted relationships with these manufacturers. Today, McKesson initiates the purchase of product through the issuance of a purchase order (PO) with the manufacturer. Upon receipt, we confirm the physical order and the data feed associated with that specific product order.

   It is our expectation that manufacturers will provide products to McKesson with GS1 compliant 2D Barcodes. McKesson has deployed a GS1 compliant traceability solution in the two California pharmaceutical distribution centers and is installing the same solution in the rest of the distribution network. We are currently using this system in the pilot projects we are conducting with manufacturers and supplying feedback to GS1 on system enhancements that should be included in the standard. This system will compare the serial numbers from the data collected from the manufacturer to the serial numbers on the products picked for the customer. Only products that have a match in our data system will be allowed to be shipped to the customer. Any products that do not match will be isolated in a quarantine area for further investigation by the shipper.

4. **If the submitting party is seeking a regulatory allowance for inference, a specific request for same along with a detailed description of the particular circumstance(s) and/or those transaction(s) under which or pursuant to which there is a perceived need for inference. Define the requested inference(s) as specifically as possible, and where possible provide a limiting descriptor for such transaction(s) that could be used in regulatory language. In addition, provide as much data as possible regarding the factual circumstance(s) and/or transaction(s) in question, including the number and percentage of transaction(s) to which such an inference might apply, both with regard**

to the submitting party and in the supply chain as a whole, and any trading partners that will be involved in the inference(s).

Inference is an important element of any implementation strategy for pharmaceutical distributors and its allowance by the Board is essential to enable distributors to meet the goals and requirements of the California law.

McKesson intends to comply with all applicable laws and plans to utilize inference in its receipt and shipment of serialized product into our distribution centers. We encourage the Board to allow us to scan the case label of a manufacturer's sealed case and match that serial number to the data provided by the manufacturer. When we have a match, we want to be able to infer that the unit serial numbers (SNI) that the manufacturer linked to the case serial number are correct. We further want to ship this sealed case to a customer or to another McKesson distribution center using inference and without a requirement to break the sealed case and read the unit level serial numbers. The vast majority of our inbound shipments come to McKesson in the manufacturers' sealed cases.

In preparation for the practice of inference, McKesson will develop a detailed standard operating procedure (SOP) to ensure that the process meets specific criteria. As with all of our distribution processes, we employ Six Sigma methodology to minimize the occurrence of errors.

5. **If the submitting party is opposed to a regulatory allowance for inference, either generally or with regard to particular circumstances/transactions, a detailed description of same that as closely as possible meets the requirements of item 4., noted above.**

   We are not opposed to regulatory allowance for inference.

6. **The detailed reason(s) that such an inference is necessary and/or advantageous, and either decreases risk(s) of diversion or counterfeiting (or other risk(s) in the supply chain), holds risk(s) constant, or does not unacceptably increase such risk(s). Or the detailed reason(s) any inference(s) is/are unnecessary, disadvantageous, or unacceptably increase(s) risk(s).**

   Ensuring the integrity of the manufacturer's case is an important safeguard. A number of our larger customers will only accept product from us in the manufacturer's sealed case. In our distribution centers, the backup stock is kept in the manufacturer's sealed case until it is brought to the picking area and prepared for picking for the customer order. When a customer orders items at the unit level, we will compare the unit serial number with the number provided to us by the manufacturer to be sure we have a valid item. Only products that have a match in our data system will be allowed to be shipped to the customer. Any products that do not match will be isolated in a quarantine area for further investigation by the shipper.

7. **Proposed SOPs that incorporate and explain the use of the inference(s), and describe the proposed process for statistical sampling to ensure the accuracy of pedigree information.**

   The industry developed a document in conjunction with GS1entitled "The Practice of Inference", which was published in 2010 and is available on the GS1 website. McKesson will base the development of its detailed standard operating procedure (SOP) for inference on this document.

8. **A proposal for the allocation of any liability that may be incurred due to use of inference.**

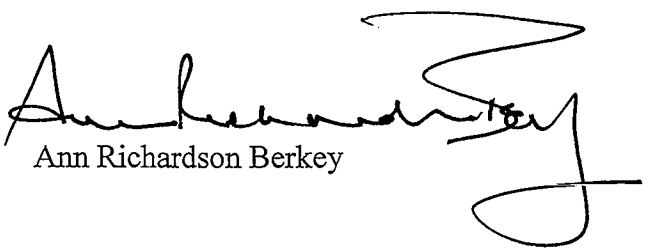
   A distributor should not be held financially liable for the accuracy of the electronic data that they receive from their supplier. Since it is likely not the intent of the packager or manufacturer of the product to improperly record the aggregation of pieces in the case, these 'honest' mistakes should be communicated to the original packager or manufacturer so that discrepancies can be addressed. When these problems are detected and a supply chain partner discovers that the serial number on the product that they currently possess does not have a proper 'chain of custody' (for example, they do not have a record that shows that they should have this product), this discrepancy must be reported to the relevant parties, including regulatory bodies. Appropriate action should be taken to either correct the situation or return the product to the manufacturer of the product.

   Any financial liability should be directed to protecting the supply chain and the detection and elimination of adulterated and counterfeit product.

On behalf of McKesson, we appreciate this opportunity to provide comments to the Board and to share our perspective regarding the use of inference to track prescription drugs. McKesson seeks to protect the integrity of the pharmaceutical supply chain while ensuring the rapid and safe delivery of medicines to patients.

We look forward to working with the Board as rulemaking on inference is further developed. Should you have any questions, please contact me or Ron Bone, Senior Vice President, Distribution Operations, McKesson Pharmaceutical, at 415-983-7613 or ron.bone@mckesson.com.

Sincerely,



Ann Richardson Berkey

MEDLINE

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Opportunity to Submit Information Necessary to Possible Board Rulemaking
On Inference and Certification of Individual Package Units – Drug Pedigree Law

The following comments are submitted on behalf of Medline Industries, Inc. We appreciate the opportunity to express our views on the importance of inference in the California pedigree system. Should the Board have any questions, please do not hesitate to contact Rob Calia at the contact information detailed below.

1. ***Identifying and contact information for the submitting person or entity.***

Company: Medline Industries, Inc.
Primary Contact: Rob Calia
Address: One Medline Place
Mundelein, IL 60060
Phone: (847) 643-4249
Email: rcalia@medline.com

2. ***A description of the submitting party's interest in this subject, including the submitting party's role, if any, in the supply chain (e.g., manufacturer, repackager, distributor, or dispenser) or other basis for interest (e.g., vendor, consultant, standards body) and a brief description of the person, company, or other entity responsible for the submission.***

Medline manufactures and distributes more than 125,000 products (including prescription drugs) to hospitals, extended care facilities, surgery centers, physician offices and home care dealers. Medline has a network of 50 manufacturing and distribution centers worldwide, including three distribution centers in the state of California.

Our interest in this subject primarily relates to our role as a wholesale distributor of pharmaceuticals.

3. ***If the submitting party is a supply chain participant, a detailed description of the means and methodology, including hardware and software specifications, processes, and data carrier(s), that the submitting party has deployed or intends to deploy to "verify and validate the delivery and receipt of dangerous drugs against [electronic] pedigrees at the unit level," including specification of the means and methodology for certification.***

In the absence of further guidance and having not yet participated in or seen the results from successful, supply chain wide, pilots, we have not yet made final determinations on the specific means and methodology we will use to comply with California's ePedigree requirements.

Medline currently uses a purchased software system to pass electronic pedigrees. We anticipate using a similar or upgraded version of this software to comply with California's ePedigree requirements.

4. ***If the submitting party is seeking a regulatory allowance for inference, a specific request for same along with a detailed description of the particular circumstance(s) and/or those***

transaction(s) under which or pursuant to which there is a perceived need for inference. Define the requested inference(s) as specifically as possible, and where possible provide a limiting descriptor for such transaction(s) that could be used in regulatory language. In addition, provide as much data as possible regarding the factual circumstance(s) and/or transaction(s) in question, including the number and percentage of transaction(s) to which such an inference might apply, both with regard to the submitting party and in the supply chain as a whole, and any trading partners that will be involved in the inference(s).

Because of the cost and unreliability of Radio Frequency Identification (RFID) technologies, we anticipate that the vast majority of manufacturers will serialize using two-dimensional matrix barcodes, which require a line of sight scan. If required to manually unpack each case and pallet and scan each individual unit, the entire pharmaceutical distribution chain will break down—endangering public health and safety by significantly exasperating drug shortages while drastically increasing the cost of pharmaceuticals for California consumers..

Therefore, we anticipate that the majority of our transactions will involve inference. We anticipate that we would utilize inference on approximately 70% of incoming product. We anticipate that we would utilize inference on approximately 15% of outgoing product.

On receipt of a product, we believe that scanning should occur at the level of product purchased (e.g. if Medline purchases a sealed case, we would scan the case and infer the Standardized Numerical Identifier (SNI) for each unit within the case). On sale of product, we believe scanning should occur at the level of product sold (e.g. if Medline sells a sealed case, the case would be scanned and inference would be used to collect the SNI for each unit within the sealed case).

With approximately 500 million prescription dispensed in California each year, we believe the only way the system can possibly function without significantly delaying the delivery of prescription drugs is to allow inference in this way.

Example 1: Medline purchases and then resells an entire pallet of drug X. Medline purchases a pallet of drug X from the manufacturer of drug X or an Authorized Distributor of Record (ADR) of drug X. Upon receipt of the pallet, Medline would use inference to collect the SNI for each individual unit contained within the pallet—leaving the pallet itself sealed. Upon resell of the sealed pallet, inference would again be used to capture the SNI from each outbound unit within the sealed pallet.

Example 2: Medline purchases a pallet of drug X, breaks down the pallet to the case level, and then sells a sealed case. Medline purchases a pallet of drug X from the manufacturer of drug X or an ADR of drug X. Upon receipt of the pallet, Medline would use inference to collect the SNI from each individual unit contained within the pallet—leaving the pallet itself sealed. When the pallet is opened for the sale of a sealed case contained within the pallet, inference would again be used to capture the SNI from each outbound unit within the sealed case.

Example 3: Medline purchases and then resells an entire case of drug X. Medline purchases a case of drug X from the manufacturer of drug X or an ADR of drug X. Upon receipt of the case, Medline would use inference to collect the SNI from each individual unit contained within the

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case—leaving the case itself sealed. Upon sale of the sealed case, inference would again be used to capture the SNI from each outbound unit with the sealed case.

Example 4: Medline purchases a case of drug X, breaks down the case to the unit level. Medline purchases a case of drug X from the manufacturer of drug X or an ADR of drug X. Upon receipt of the case, Medline would use inference to collect the SNI from each individual unit contained within the case—leaving the case itself sealed. When the case is opened for the sale of an individual unit(s), individual units will be scanned to capture the SNI.

5. ***If the submitting party is opposed to a regulatory allowance for inference, either generally or with regard to particular circumstances/transactions, a detailed description of same that as closely as possible meets the requirements of item 4., above.***

   Medline supports the use of inference, as described above.

6. ***The detailed reason(s) that such an inference is necessary and/or advantageous, and either decreases risk(s) of diversion or counterfeiting (or other risk(s) in the supply chain), holds risk(s) constant, or does not unacceptably increase such risk(s). Or the detailed reason(s) any inference(s) is/are unnecessary, disadvantageous, or unacceptably increase(s) risk(s).***

   We believe that inference can be used in the ways described above without increasing the risk of diversion or counterfeiting (or other risks(s) in the supply chain) and may in fact reduce some supply chain risks.

7. ***Proposed SOPs that incorporate and explain the use of the inference(s), and describe the proposed process for statistical sampling to ensure the accuracy of pedigree information.***

   Our SOPs will be shaped by the statutorily mandated regulations under development by the Board. In the absence of these regulations and without a more complete understanding of how manufacturers will utilize inference and aggregation Medline is unable to craft detailed SOPs.

8. ***A proposal for the allocation of any liability that may be incurred due to use of inference.***

   We believe any liability that may be incurred due to the use of inference should be assumed by the aggregator—e.g. the manufacturer or repackager. The aggregator is the one who makes and certifies the aggregation which those further down the supply chain must rely upon. Should there be any issues with that initial aggregation/inference, the manufacturer or repackager who made it should be fully liable.

The Pharmaceutical Distribution Security Alliance

Response to the California State Board of Pharmacy

Regarding Inference and Certification of Individual Package Units

INTRODUCTION

The Pharmaceutical Distribution Security Alliance (PDSA) appreciates the opportunity to submit these comments in response to the request of the California State Board of Pharmacy (the Board) for information necessary to any Board rulemaking on inference and certification of individual package units – drug pedigree law (Bus. & Prof. Code, §§ 4034, 4163 et seq.).

PDSA's mission is to develop and help enact a federal policy proposal that enhances the security and integrity of the domestic pharmaceutical distribution chain for patients, and to articulate a technical migratory pathway to implement such a policy. Our primary goal is ensuring patients have uninterrupted access to safe, authentic, U.S. Food and Drug Administration (FDA)-approved medicine. Membership of PDSA spans the entire spectrum of the U.S. pharmaceutical distribution chain, including manufacturers, wholesale distributors, third-party logistics providers, and pharmacies. Twenty-nine organizations are formal members of PDSA, while many other external stakeholders provide additional policy and technical support to the group. Please see the "About Us" document attached for more information about the submitting party, including contact information for PDSA.

While we are fortunate to live in a nation where the pharmaceutical distribution chain is relatively safe, grave threats from sophisticated criminal elements still exist, and are becoming more severe. PDSA appreciates the efforts of the Board to protect California consumers by preventing, assessing, and responding to threats of prescription drug counterfeiting and diversion in the state supply chain. We agree with the Board, FDA and other stakeholders that more must be done to protect U.S. patients from these public health threats.

RESPONSE[1]

The ability to use or rely on inference(s) as to the contents of aggregate containers for purposes of certification of delivery or receipt of individual package units of prescription drugs is operationally essential to facilitate the efficient movement of prescription drugs in California.

We encourage the Board to carefully consider the technical input from the many diverse participants in the distribution chain, whose abilities and needs may vary depending on the nature and scope of their operations and the California populations they serve. PDSA, with membership representing a broad spectrum of distribution chain participants, fully appreciates the difficulty of crafting policies and rules that will be feasible for all stakeholders – but striking this balance is essential when seeking to craft a comprehensive supply chain security system, as the chain is only as strong as its weakest link. We encourage the Board to remain highly attuned to this challenge as it considers possible rulemaking.

The California statute will require the creation of a substantial interoperable electronic system to connect the thousands of unique participants in the pharmaceutical distribution chain to enable tracking and tracing all individual prescription drug product packages at the smallest saleable unit ("unit") through use of "electronic pedigrees" (e-pedigree) showing the full distribution history of each

[1] Separate and distinct from these comments, PDSA members may also opt to respond to the Board's request for information in their individual capacity. Any such response should not be construed to reflect the views of PDSA.

individual unit sold in the state. Creating such a system that consistently and efficiently works for the thousands of small and large entities in the distribution chain – including drug manufacturers, wholesale distributors, third-party logistics providers, and retail, independent, hospital and clinic pharmacies – is a novel, complex, expensive, and highly technical undertaking. Accordingly, PDSA appreciates the Board's recognition that technical input from distribution chain participants is essential to the development and implementation of a new pharmaceutical distribution system.

While we fully expect that all legitimate companies interested in continuing to do business in California will seek to comply with the e-pedigree law, we recognize the substantial challenges in doing so. As such, it is critical to establish an interoperable electronic system that meets an industry accepted standard that connects all trading partners and allows for the reliable and efficient exchange of e-pedigree data in order for companies to be able to comply with the California law.

A. Compliance with the California Law Requires a Workable Interoperable Electronic System

Functional technology and interoperability is the foundation of the envisioned California e-pedigree system, and is the essential first step for companies seeking to comply with the law. While regulations on inference and certification are important to creating a functional e-pedigree system, without a workable interoperable electronic system as the starting point, even the most consensus driven regulations would be of limited utility.

To enable companies to comply with the California law, the interoperable electronic system must function for every one of the thousands of entities in the pharmaceutical distribution chain operating and doing business in California. Unless all can do it, the ability of only some (or even most) companies and healthcare entities to exchange e-pedigree data will be negate the intended results as the required chain of ownership would be broken in many instances. Simply put, unless the e-pedigree system works for all of us, it works for none of us, and interoperable exchange of e-pedigree data is the keystone to the CA system.

B. Concerns with the Current State of E-Pedigree Technology and Interoperability

The envisioned California e-pedigree system relies on an interoperable electronic system(s) that connects all trading partners and ensures an efficient and secure exchange of e-pedigree information. Though efforts to create such a system are ongoing, no such system currently exists for all participants in the chain, and industry discussion and debate about the most efficient and effective model continues. This creates significant compliance challenges that cannot quickly or easily be overcome:

- The development of standards for information exchange and business process for data management (including protocols regarding master data and exceptions management), and the reliable use of vendor systems takes time and testing. Even if these pieces were in place for manufacturers, all downstream partners must also have an interoperable system including the availability and testing of the necessary standards in place to exchange serial numbers, e-pedigrees, and associated transaction information (i.e. from shipments, receipts, returns, etc).
- Despite many stakeholders' attempts to build systems to comply with the e-pedigree law, there is very little data to estimate expected failure rates. As an example: for just one company , even a 99% accuracy rate would result in exceptions impacting 550,000 units each year, meaning approximately 2,201 items per day could enter the supply chain and would be inaccurate, thereby compromising the integrity of the system. Moreover, any of the errors that surface could sit in quarantine awaiting resolution. If each company along the supply chain experiences 1% or even higher failure rates, the amount of possibly inaccurate and possibly quarantined

product is further increased. If current pilot projects' accuracy rates do not improve, the distribution of many thousands of products would be inaccurate and could be delayed. Such findings highlight the need for extensive testing of this functionality across all products, all trading partners, and all shipping/receiving points well in advance of the effective date of such a requirement.

- In another company's pilot, the inference concept was tested in small application, using transactions containing roughly 10,000 serialized units. The pilot used 2D and 1D GS1 standards barcodes with aggregation of unit to case, case to pallet relationships. When the data exchanged were 100% accurate to the labels for the product, inference did work. However, when technical exception issues occurred – which many did – it either took tremendous time to correct the problem or it could not be corrected at all. In this pilot, most of transactions required some level of human intervention to correct technical issues; less than 10% went through without error.
- Implementation of an interoperable electronic system is complicated by the fact that many trading partners have varying legacy systems, different solutions providers, and significantly different resources and capabilities to effectively deploy and test such a system.

While it is concerning that liabilities may be imposed on legitimate pharmaceutical distribution chain participants not capable of meeting unproven expectations, technical challenges are not merely issues that impact corporate compliance. Accuracy and interoperability – and in this case the lack thereof – can compromise the integrity of the system and potentially impact patient access to medication and the public health. According to IMS 2010 data, approximately 638,400,000 prescriptions are dispensed to patients in California each year, and these products reach consumers through many more millions of transactions in the pharmaceutical distribution chain. If any part of the complex e-pedigree process fails – even if only for technological reasons – the prescription drug cannot be distributed, resulting in possibly dangerous delays or limited supplies in medications available to patients due to slower distribution schedules and large-scale product returns. We trust that all stakeholders will actively work to avoid such outcomes that endanger the public health while also seeking to comply with the California law.

CONCLUSION

While we agree with the Board's intent to enhance patient safety, PDSA respectfully urges the Board to consider the important prerequisite of proving the functionality and reliability of the interoperable electronic system for all participants in the pharmaceutical distribution chain. Such is the essential first step for companies seeking to comply with the California law and is critical for ensuring system accuracy and integrity so that patients will continue to have timely, efficient access to prescription medications.

Thank you for your consideration.

The Pharmaceutical Distribution Security Alliance

Attachment: PDSA "About Us" Document

Pharmaceutical Distribution Security Alliance (PDSA)

Our Mission

The Pharmaceutical Distribution Security Alliance's (PDSA) mission is to develop and help enact a federal policy proposal that enhances the security and integrity of the domestic pharmaceutical distribution system for patients, and to articulate a technical migratory pathway to implement such a policy. Our primary goal is ensuring patients have uninterrupted access to safe, authentic, FDA-approved medicine.

About Us

The Pharmaceutical Distribution Security Alliance is a multi-stakeholder and interdisciplinary initiative. Membership spans the entire spectrum of the U.S. pharmaceutical distribution system, including manufacturers, wholesale distributors, third-party logistics pro viders, and pharmacies. More than 20 companies are formal members of PDSA, while many other external stakeholders provide additional policy and technical support to the group.

Membership

For more information about the PDSA or this document, please contact:

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Comments Submitted Re: Inference and Certification of Individual Package Unit

Pharmacies

CSHP | CALIFORNIA SOCIETY OF HEALTH-SYSTEM PHARMACISTS
Partners in Medication Management

August 29, 2012

Virginia Herold
Executive Officer, California State Board of Pharmacy
1625 North Market Blvd, Suite N219
Sacramento, CA 95834

Dear Ms. Herold;

Thank you for the opportunity to comment on the Drug Pedigree Law as it relates to inference and certification of individual package units.

As licensed healthcare practitioners in California, we support the Board's decision on moving forward with Pedigree Law to protect the public from counterfeit medications and minimize drug diversion. Furthermore, we concur with the California Society of Health-System Pharmacists (CSHP) Policy on E-Pedigree and Tracking of the Medication Supply Chain (see Attachment 1). While many of the processes for ordering, receiving, and inventorying of pharmaceuticals are shared across pharmacy practice settings (community, hospital, retail, etc.), the Pedigree Law will create unique challenges and opportunities for hospital pharmacists. We wish to elucidate the specific implications of the Pedigree Law on inpatient pharmacy practice.

To facilitate electronic inference, it is expected that all firms fulfilling orders of dangerous drugs in aggregate containers will assign serial numbers to their containers as below:

- The aggregate is identified with a unique serial number and each unit/item in the aggregate is also identified with a unique serial number. For example, if medications are received in a pallet, then each pallet will have unique serial number, each tote on the pallet will have a unique serial number, and each unit in the tote will have its own unique serial number.
- All serial numbers are associated with the aggregate in a hierarchical relationship.
- Electronic communication identifies each item in the aggregate.
- Pharmacies will have assurance that the integrity of the aggregate has remained intact since leaving the last supply chain partner and can confirm the integrity of the aggregate has not been compromised.

1) Risks Associated with Open Cases

We support a regulatory allowance that would allow individual pharmacies to choose to infer the contents of aggregate containers for the purposes of certification of delivery or receipt of individual package units for all dangerous drugs. Inference supports patient safety, security and efficiency in the supply chain distribution process (i.e., products move faster in the supply chain). Opening containers to verify the individual package can lead to:

- Delayed delivery of medications to patients
- Introduction of error into the system
- Tampering
- Theft
- Product mix-up

The security and integrity of medications may be compromised if security seals or tamper evident packages are not left intact. For example, open packages of controlled substances may lead to tampering or theft.

2) Statistical Sampling

We support statistical sampling of incoming shipments from trusted members of the supply chain rather than conducting 100% inspection of all incoming items to assess the presence and integrity of the products. We do not support regulatory language which would require pharmacies to perform sampling for chemical analysis of medications; rather, sampling should be limited to product or package confirmation. We would recommend each Pharmacist in Charge (PIC) be responsible for delineating within their own Standard Operating Procedures (SOPs):

- Frequency and amount of sampling performed.
- Situations in which 100% of the shipment should be inspected if there is reason to be suspicious about the integrity of an incoming shipment.

Manufacturers and distributors/wholesalers should have additional responsibility for conducting more frequent statistical sampling (based on the Acceptable Quality Level [AQL]) and periodic chemical analysis before medications are shipped to pharmacies. Pharmacies should not be liable for receiving counterfeit or mishandled medications during transportation.

3) Technology and Manual Pedigree

We anticipate the Board will receive comments from other supply chain participants and technology vendors with specific hardware, software, and data carrier recommendations to facilitate the passing of electronic pedigree information among supply chain participants. We believe the system used for tracking E-Pedigree should be harmonized with internationally recognized standards for such an identifier (e.g., Radio Frequency Identification (RFID), Serialized Global Trade Item Number (SGTIN)). We urge the Board to recognize there will be situations which will require manual tracking of pedigree information (e.g., during hardware/software downtime, emergency situations). We suggest each hospital should define within their SOPs their process for manual pedigree tracking. Ideally, in the future, one machine-readable code would contain a product's expiration date, lot number, and NDC number which would be then tracked through pedigree.

4) Exception for Using Electronic Pedigree (Risk Assessment)

While the comments above are specific to the use of inference of aggregate package contents, the situations in which an electronic pedigree must be passed between supply chain participants impacts and will be impacted by the decision to use inference. Because of the difficulties associated with passing an E-pedigree, the relationships hospital pharmacies have with the entities below, and the minimal risk of tampering, fraud or errors, we recommend against the use of electronic pedigrees in the following situations:

- The ability for pharmacies to procure essential medication from another pharmacy to avoid patient harm (i.e., emergency loan and borrow)
- Sales/transfers to another pharmacy under common control
- Sales/transfers to authorized providers (e.g., sales to private doctors' offices)
- Medication shipments approved by the FDA and received from outside of the United States due to critical drug shortages (e.g., methotrexate from Europe)
- Reverse distributor transactions (e.g., for expired and recalled medications)
- Compounded medications from contracted pharmacies that have a quality assurance program built in as part of their contracted relationship with the pharmacy (e.g., outsourced parenteral nutrition compounding company)
- Existing medication inventory

Finally, we would appreciate the opportunity to address these issues at an upcoming Board meeting.

Founded in 1962, CSHP represents over 4,500 pharmacists, student pharmacists, pharmacy technicians, and associates who serve patients and the public through the promotion of wellness and rational drug therapy. CSHP members practice in a variety of organized healthcare settings – including, but not limited to, hospitals, integrated healthcare systems, medication therapy management clinics, home healthcare and ambulatory care settings.

If you have any questions and/or comments, please do not hesitate to contact me or CSHP Legislative and Regulatory Analyst Jonathan Nelson at (916) 447-1033 ext. 105 or jonathan@cshp.org.

Sincerely,

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Executive Vice President/CEO
California Society of Health-System Pharmacists
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CSHP | CALIFORNIA SOCIETY OF HEALTH-SYSTEM PHARMACISTS
Partners in Medication Management

Attachment 1

California Society of Health-System Pharmacists (CSHP) Policy on
E-Pedigree and Tracking of the Medication Supply Chain

CSHP advocates for improved processes to assure the integrity of medications throughout the supply chain, specifically to eliminate or minimize the persistent and increasing threat from counterfeit, misbranded, adulterated, or diverted drugs.

1. Support the California State Board of Pharmacy in development of a comprehensive electronic pedigree system to track and trace the passage of medications through the entire supply chain.
2. Require the technology and process implemented be compatible with national and international standards so as not to impede the supply of medications.
3. Require the technology(s) adopted must be a single, shared interoperable system to allow health-systems to receive medications from all sources in a single process.
4. Advocate that the technology developed has the future ability to extend the validation of the pedigree to the level of patient administration throughout the continuum of care.
5. Assure that health-systems be an active participant in the development of technology, process design and implementation.
6. Advocate that the implementation deadlines for the supply chain be a phased in approach allowing health-systems time to implement after the deadlines for manufacturers and distributors.
7. Require that "grandfathered" inventory be addressed in the implementation plan to minimize inventory losses.
8. Advocate for a streamlined process to allow medication returns and "emergency" borrowing of medications within the documentation process.

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NACDS NATIONAL ASSOCIATION OF CHAIN DRUG STORES
CALIFORNIA RETAILERS ASSOCIATION
980 Ninth Street, Suite 2100 Sacramento, CA 95814
(916) 443-1975 calretailers.com
california pharmacists association

August 29, 2012

Virginia Herold
Executive Officer
California Board of Pharmacy
1625 North Market Blvd., Suite N219
Sacramento, CA 95834

RE: Comments regarding Inference and Certification of Individual Package Units – Drug Pedigree Law

Dear Executive Officer Herold:

The California Retailers Association (CRA), the California Pharmacist Association (CPhA) and the National Association of Chain Drug Stores (NACDS) thank the Board of Pharmacy ("Board") for the opportunity to submit written comments in response to the Board's request for information regarding supply chain participants' ability to use or rely on inference(s) as to the contents of aggregate containers for purposes of certification of delivery or receipt of individual package units of dangerous drugs, as required by the California electronic pedigree law.

The retail community pharmacy industry is committed to maintaining and enhancing the safety and security of the U.S. drug distribution supply chain through feasible and workable means. We believe that the United States prescription drug distribution system is one of the safest in the world, if not the safest. A number of proactive safety measures in the private sector and a comprehensive set of federal and state laws and regulations contribute to this safety. We are proud of the private sector initiatives that our members have taken along with other industry stakeholders to enhance the security of the U.S. drug supply chain. Retail community pharmacies have made changes in their purchasing practices, such as requiring their wholesale distributors to purchase prescription drug products directly from manufacturers. This policy creates a secure system of distribution known as the "normal distribution channel" -- a direct flow of product from the manufacturer to the wholesale distributor, and to the pharmacy for dispensing.

Contact Information
The contact information for the submitting entities and persons are provided at the conclusion of this letter.

Submitting Parties' Interest in this Subject
CRA is a statewide trade association representing all segments of the retail industry including chain drug stores. CPhA is the largest statewide pharmacy association in the country, with over 5,000 members practicing in all practice settings. Additionally, CPhA represents nearly 1,000 independent community pharmacies operating throughout California. NACDS represents traditional drug stores, supermarkets, and mass merchants with pharmacies – from regional chains with four stores to national companies. Chains operate more than 40,000 pharmacies and employ more than 3.5 million employees, including130,000 pharmacists. Our members dispense over 2.6

billion prescriptions annually, which is more than 72 percent of annual prescriptions in the United States. In the state of California, NACDS represents 20 companies operating 3,916 pharmacies.

Reasons Inference is Necessary and Advantageous
While we continue to have concerns about the necessity and effectiveness of extending electronic pedigree requirements to individual community pharmacies, we believe that allowing inference is a significant and necessary component for maintaining supply chain integrity under California's electronic pedigree law. Inference must be available for use by pharmacies and other supply chain participants. Allowing inference at the pallet, case, and tote levels is critical to preserve supply chain security and enhance patient safety by preserving the integrity of the pallet, case, tote or other aggregated distribution unit.

Without inference, it is highly likely that the aggregated product, e.g. pallets, cases, totes, would need to be opened, creating the potential for loss of product, diversion, and risks to the safety and security of the supply chain. We believe that inference has the potential to decrease the risk of diversion and enhance security and safety by maintaining the integrity of the aggregated containers.

Without inference, each pallet, case, or tote would have to be opened and each individual drug package scanned. This would lead to an inefficient, costly, and time consuming process that would cripple the entire drug distribution supply chain. Without inference, the supply chain will likely see insurmountable product delays from having to manually scan millions of products. As a result, pharmacies will have difficulties meeting the medication needs of their patients. Moreover, opening up the boxes or containers for scanning will destroy the security of the sealed containers. Imposing such an inefficient time-consuming system on pharmacies and other healthcare providers makes little sense.

Proposed Standard Operating Procedures
At this time to our knowledge, due to the very limited availability and use of serialized prescription drug product packages, we believe that standard operating procedures are under development. As associations that representing retail community pharmacists and pharmacies, we look forward to the development and review of such procedures as they are made available. We defer our comment until that time.

Liability
In regards to liability, we believe that liability has little usefulness in the area of inference. However, we certainly believe that pharmacies should not be held liable for inaccurate packing by the wholesaler or manufacturer. Rather, we believe that the better approach is to understand the complexities of this as yet untried and untested system, and therefore to allow supply chain stakeholders to exist in a learning environment. This system is not in use in California and is being built from the ground up. As such, we recommend that liability be forestalled as stakeholders learn this new system.

Conclusion
Although our concerns remain about the feasibility and workability of California's electronic pedigree law, we support inference and believe that it is a critical component of the electronic pedigree process. Please do not hesitate to contact Mandy Lee with the CRA at mlee@calretailers.com or 916-425-8481, Brian Warren with CPhA at bwarren@cpha.com or 916.779.4517, or Mary Staples with NACDS at mstaples@nacds.org or 817.442.1155 if we can provide further assistance.

Sincerely,

Mandy Lee
Director of Government Affairs
California Retailers Association

Mary Staples
Director of Government Affairs
National Association of Chain Drug Stores

Brian Warren
Director of Government & Professional Affairs
California Pharmacists Association

Comments Submitted Re:
Inference and Certification of
Individual Package Unit

Other

National Council for Prescription Drug Programs
NCPDP

August 27, 2012

California State Board of Pharmacy
1625 N Market Blvd.
Suite N219
Sacramento, CA 95834

Re: **Opportunity to Submit Information Necessary to Possible Board Rulemaking On Inference and Certification of Individual Package Units – Drug Pedigree Law**

Dear Board of Pharmacy:

NCPDP is a non-profit ANSI-accredited Standards Development Organization consisting of more than 1,600 members who represent computer companies, drug manufacturers, pharmacy chains and independents, drug distributers, insurers, mail order prescription drug companies, pharmaceutical claims processors, physician services organizations, prescription drug providers, software vendors, telecommunication vendors, service organizations, government agencies and other parties interested in electronic standardization within the pharmacy services sector of the health care industry.

NCPDP and its membership are interested in a safe, secure and efficient supply chain for drugs and biological products.

NCPDP Response:
The stated goal of the pedigree regulation is to establish and implement a system to ensure patient safety and improve the security of the drug supply chain against counterfeit, diverted, sub potent, substandard, adulterated, misbranded, or expired drugs. Inference is essential to the practical achievement of this goal.

Inference, as it is currently used within the supply chain, supports both the security of the product being shipped and the efficiency of the supply chain. The manufacturer/repackager, following established security protocols, seals and places the identifier on a case (or higher level shipping container) of medication prior to shipping. So long as that seal is unbroken, the downstream trading partners can trust, i.e. infer, that content received is the content packed by the manufacturer/repackager. If an error is found on opening the container at the point of use, then it can be reported back to the manufacturer/repackager and the product quarantined until the problem is resolved.

To not use inference, that is, to inspect the contents of every case as it moves through the supply chain, would dramatically slow the movement of products, but more importantly, it would substantially increase the opportunity for substitution and diversion. If a problem is found at the point of use, there is no way to pinpoint where it occurred since the integrity of the case was not maintained to the final destination.

Conclusion
Inference allows a reasonable level of security with a lower expenditure of resources and may even protect the supply chain from introduction of adulterated, misbranded or counterfeit product that could otherwise be missed due to the massive number of reviews that would be required. Therefore, the use of inference can provide the necessary protection while allowing the reasonable flow of product through the drug distribution chain.

Enhancing the safety and security of the prescription drug supply chain is of acute interest to NCPDP and its members. For the last four years NCPDP Work Group 17 Pharmaceutical Pedigree and Traceability has explored the many facets of pedigree, track and trace regulations and other potentially inter-related pharmacy technology initiatives. Based on our experience with the successful implementation of networked systems, NCPDP understands the magnitude of developing and implementing a track and trace system.

NCPDP stands ready to assist the CA Board of Pharmacy in achieving consensus and support within the pharmaceutical industry for the development and implementation regulations to enhance the safety and security of the drug supply chain.

Thank you for the opportunity to respond to this request for comments.

For direct inquiries or questions related to this letter, please contact
Sue Ann Thompson
Standards Advisor, NCPDP
Direct:
3737 Tug Fork RD
Ripley, WV 25271
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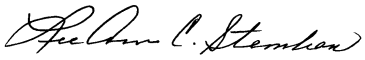
sthompson@ncpdp.org

Sincerely,



Lee Ann C. Stember
President
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9240 E. Raintree Drive
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(480) 477-1000 x 108
lstember@ncpdp.org
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cc: NCPDP Board of Trustees

Attachment II(e)

California State Board of Pharmacy
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Fax: (916) 574-8618
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Attachment II(e): Proposed Enforcement Committee meeting dates for 2013.

- March 5 (Most likely in the Bay Area)
- June 4 (Southern CA)
- September 10
- December 3